PHARMACY MATERIAL FOR COMPETITIVE EXAMS

(Will update next month with new chapters)

- Government Pharmacists Jobs
- Drug Inspector Jobs
- GPAT, PGECET, NIPER and other competitive Exams

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PHARMACOGNOSY

CARBOHYDRATES:

Carbohydrates are polyhydroxy aldehydes or ketones that on hydrolysis give aldehyde or ketone compounds.

Monosaccharides: Monosaccharides cannot hydrolysed to simple sugars.

- Bioses contain two carbon atoms, but not available on natural.
- Triose contain 3 C atoms, but in phosphoric esters ex: Glyceraldehyde
- Tetrose contain 4 C atoms Ex: Erythrose
- Pentose contain 5 C atoms Ex: Arabinose, Ribose, Xylose
- Hexose contain 6 C atoms, these are divided as Aldoses (Glucose, galactose, and galactose) and Ketoses (Fructose & sorbose)

Disaccharides: Upon hydrolysis gives monosaccharides. Ex: Sucrose, Maltose, Lactose.

- Sucrose on hydrolysis gives Glucose + Fructose
- Maltose on hydrolysis gives glucose + glucose
- Lactose on hydrolysis gives glucose + galactose

Trisaccharides: On hydrolysis gives 3 molecules of monosaccharides.

- Raffinose gives glucose + fructose + galactose
- Gentianose gives glucose + glucose + fructose.

Tetrasaccharides: On hydrolysis gives four molecules of monosaccharides. Ex Stachyose.

Polysaccharides: On hydrolysis give more number of monosaccharides. These can be divided as Pentosan (xylan) & hexosans (starch, inulin and cellulose).

- Cellulose is composed of glucose units joined by β-1,4 linkages.
- Starch contains glucose units α-1,4; α-1,6 units

- Gums are pathological products consisting of Ca, K and Mg salts of complex substances known as Polyuronides.
- Mucilages are physiological products related to gums and they are sulphuric acid esters.

Drug Name & synonym	Biological Source	Chemical constituents	Uses
Acacia (Indian gum, Gum Arabica)	Stem & branches of Acacia Arabica F: Leguminosae	Arabin (mix of Ca, Mg & K salts of Arabic acid), Peroxidase	Demulcent, suspending & emulsifying agent
Guar Gum (Jaguar Gum)	Endosperm of seeds of Cyamopsis tetragonolobus F: Leguminosae	Gauran	Binding & disintegrating agent, bulk laxative, suppress appetite
Honey (Madhu, Mel)	Sugar secretion deposited by Apis mellifera F:Apidae	Glucose, fructose, sucrose	Demulcent, sweetening agent
Gum Tragacanth	Stem & branches of Astragalus gummifer F:Leguminosae	Tragacanthin (water soluble), Bassorin	Demulcent, thickening,suspending & binding agent
Sodium Alginate	Sea weed (Algae) of Macrocystis, Laminaria, Ascohyllum	Alginic acid	Suspending & thickening agent, binding & disintegratingagent
Pectin	Inner portion of rind of citrus fruits F:Rutaceae	Pectin	Adsorbent in treatment of diarrhea, hemostatic
Gum Ghatti	Anogeissus latifolia F:Combretaceae	Ca & Mg salt of gum, Peroxidase	Emulsifying agent
Gum Karaya (Indian tragacanth)	Stem of Sterculia urens F:Sterculiaceae	Polysaccharide of acetyl group & uronic acids	Bulk laxative, denture adhesive, emulsifier, thickener
Chitin	Skeletal material of invertebrates	2-acetamido 2-deoxycellulose	Used in wound healing preparation,
Ispaghula, Indian Psyllium, Isabgol	seeds & husk of Plantago ovata F: Plantaginaceae	Mucilage consists pentosan & aldobionic acid	Demulcent, laxative, in dysentery, chronic constipation,
Bael, Bengal Quince	Fruits of Aegle Marmelos F:Rutaceae	Marmelosin (a furocoumarin), Vitamin A &C	Digestive, appetizer, in treatment of diarrhea,dysentery
Agar, Japanese	Red algae of Gelidium	Agarose,	Emulsifying & bulk

Isinglass, Vegetable gelatin	amansi (Gelidaceae), Gracilaria (Gracilariaceae)	Agaropectin	laxative, used in bacteriological culture
Carrageenan (Irish moss extract)	Sea weed (red algae) of chondrus crispus F:Rhodophyceae	Kappa & lambda carrageenan	Emulsiying & stabilizing agent
Manna	Stem of Fraxinus ornus F:Oleaceae	Mannitol, Mannotriose, fraxin	Laxative
Mannitol	Reduction of Mannose		Osmotic diuretic, diluents,thickening agent,
Inulin,Dehlia	Bulb of Inula helenium, root of chicorium intybus F:Compositae	Polysaccharide of 35-50, 1-2 linked fructo-furanose units	Diagnostic agent, used in culture media,
Xantham Gum	Fermentation of glucose by Xanthomonoas compestris	Chain of D-glucose,D-mannose, D-glucoronic acid	Emulsifying agent, stabilizer, thickener
Locust Bean Gum (Carob gum)	Endosperm of seeds of Ceratonia siliqua F:Leguminosae	D-galacto-D-mannoglycan	Stabiliser, thickener, binder in cosmetics.
Dextrin(British gum, Starch gum)	Incomplete hydrolysis of starch with dilute acids		In tablet excipient
Dextran	Obtained by growing bacteria(Leuconostoc) on sucrose		Plasma volume expander, Dextran 40 as blood flow adjuvant
Starch (Amylum)	Grains of Zea Mays (Maize), rice (Oryza), wheat (Triticum) F:Graminae Potato (Solanum tuberosum F:Leguminose	Amylose (water soluble), Amylopectin (water insoluble)	Demulcent, protective, absorbent, antidote in iodine poisoning, diluents, disintegrating agent
Liquid Glucose (Corn syrup)	Partial hydrolysis of starch by HCl	D-glucose, maltose dextrin, water	Sweetening agent, not used in instead of glucose in iv prep,
Caramel (Burnt sugar)	Heating sucrose/glucose by Na_2CO_3 or mineral acid	-	Colourant in food industry, in elixirs, syrups
Arrow Root Starch (West Indian)	Rhizomes of Maranta arundinacee F: marantaceae	-	-

Arrow Root Starch (East Indian) Curcuma starch	Rhizome of curcuma angustifolia F: Zingiberace		Pharmaceutical aid
Echinacea (Black Sampson, cone flower)	Underground parts of Echinacea purpurea F:Asteraceae	Arabinoglycan, fucogalactoxyglucan	Immunostimulant, used in treatment of viral infections (cold & FLU), antiseptic & peripheral vasodilator

CHEMICAL TESTS OF CARBOHYDRATES:

Molisch's Test: Treating compound with α-naphthol and concentrated sulphuric acid gives purple color.

Fehling's Solution: Solution of compound, add equal quantity of Fehling's A & B, after heating brick red precipitate is obtained. (Reduction)

Specific Tests:

Drug	TEST	Result
Acacia	With Lead subacetate	Gelatinization
	Solution of ruthenium red	Does not give pink color
	Addition of H_2O_2 & benzidine in alcohol to the gum solution	Gives Blue color due to oxidase enzyme
Guargum	Weak Iodine solution	Does not give olive green color
	Solution of ruthenium red	Does not give pink color
	2% Lead acetate	Precipitate forms
	Addition of H_2O_2 & benzidine in alcohol to the gum solution	Gives Blue color due to oxidase enzyme
Honey (Adulteration test)	Fiehe's Test for detecting artificial invert sugar (add resorcinol in HCl to honey)	Instant red color due to furfural
Tragacanth	Boil with 10% $FeCl_3$ solution	Deep yellow precipitate
	Gum solution with precipitated CuO in conc NH_4OH	Stingy Precipitate formed
	Warm with NaOH	Canary yellow color
	Warm with Iodine solution	Green color

Alginic acid	Aqu solution with $CaCl_2$	Copious precipitate
	1% solution with dil H_2SO_4	Heavy gelatinous precipitate
Pectin	To 1% Solution, add 1 ml 2% KOH +HCl	Colorless gelatinous precipitate forms
Gum Ghatti	Millon's reagent	Fine precipitate
	With Lead subacetate	Slight precipitate
	2%gelatinous solution in water	Precipitate
CHITIN	Soak chitosan in I_2 solution add 10% H_2SO_4	Deep violet color developed
	Chitosan in HNO_3	Sphero-crystals formed, when examined by polarized light distinct cross observed
ISAPGOL	Ruthenium red	Pink Color
	Swelling Factor	For seeds is 10-14
AGAR	Boil with 100ml water	Forms stiff jelly
	Ruthenium red	Pink color
	With tannic acid	No precipitate produced
Locust Bean gum	With 5% KOH solution	Clear solution formed
Starch	Boil with water	Translucent viscous jelly
	By above jelly, add Iodine	Blue color disappears on warming

Microscopic Characters of various Starch sources:

RICE STARCH	Granules are simple/compound. Simple granules are polyhedral, 2-12 µ. Compound granules are ovoid & 12-30 micron in size. Contain 2-150 components.
Wheat Starch	Simple lenticular circular/oval granules in 5-50µ size, granules contain hilum at centre with striations. Contain 2-4 components
Maize Starch	Polyhedral/rounded granules 5-31 in size, with distinct cavity in centre 2-5 rays cleft
Potato Starch	Simple granules with ovoid/sub-spherical shape, with 30-100 µ. Hilum is present near narrower end with good concentric striations

ADULTERANTS:

Crude Drug	Adulterant	Characteristics
Indian Gum	Gum ghatti, starch, dextrin	Acacia gum is glossy, brittle in nature, pieces of broken tears are angular fragments
Honey	Artificial invert sugar	Fiehe's test
Isapgol (Plantago ovata)	Plantago lanceolata	P lanceolata seeds are oblong, elliptical in shape, swelling factor is only 5

GLYCOSIDES

Glycosides are organic compounds from plants or animal resources which on enzymatic or acid hydrolysis give one or more sugar moieties (glycone part) and nonsugar moiety (aglycone part).

- Glycosides are formed by interaction of hydroxyl group each of sugar and non sugar moiety, with a loss of water molecule (Glycosidic linkage: OH group of glycone and H group of Aglycone).

Based on hydrogen group of aglycon come from CH, OH, SH and NH, Glycosides can be classified as:

C-Glycosides: Ex: Anthraquinone glycosides cascarosides, aloin, flavones type of glycosides. They hydrolysed by oxidative hydrolysis with Ferric Chloride but not by heating with dilute acids/alkalies.

O-Glycosides: They are hydrolysed by heating with dilute acids/alkalies.Ex: Senna, Rhubarb.

S-Glycosides: They formed by interaction of sulfhydryl group of aglycone and hydroxyl group of glycone.Ex: isothiocyante glycosides like Sinigrin

N-Glycosides: Ex:Nuclosides

Drug	Biological source	Chemical constituents	Uses
ANTHRACENE GLYCOSIDES			
Senna leaf (Indian or Tinnevelly Senna, Senai Ki patti	Dried leaflets of *Cassia angustiolia* F:Leguminosae	Sennosides A & B (Aglycone is Rhein Dianthrone)	Purgative
Alexandrian Senna	*Cassia acutiolia*	As above	Purgative
Aloes (Kumari, Musabbar) F: **Liliacaeae**	*Aloe Baradensis (Curacao)* *Aloe Perri (Socotrine)* *Aloe Ferox* *Aloe Spicata (Cape aloes)*	Aloin is a mix of glucosides nmajorly Barbaloin main constituent,β-Baraloin	Purgative, anti-wrinkle property, in keratosis
Rhubarb (Rheum, Revandchini)	*Rhizomes of Rheum emodi (Indian), R.webbianum (Chinese)***F:Polygonaceae**	Rhien, emodin, Aloe emodin, palmidin A, B & C, chyrsophanol	Bitter stomachic & in diarrhea, purgative
Cascara (sacred bark, chittem bark)	*Bark of Rhamnus purshiana F:**Rhamnaceae***	Cascarosides A,B,C & D; barbaloin, emodin etc	Stomachic, tonic & purgative
Hypericum (St John Wort, Goat weed)	*Aerial parts of Hypericum perforatum F:**Hypericace***	Hypericin, hyperforin pseudohypericin,	Anti depressant, neuralgia ibrocitis, sciatica, in HIV
Cochineal (Red scale insect,coccus)	*Female insects,larvae of Coccus cacti F: **Coccidae***	Carminic acid	Coloring agent
STEROL or CARDIAC GLYCOSIDES			
Digitalis/Foxglove Leaves	*Leaves of Digitalis purpurea F:**Scrophulariace***	Purpurea glycosides A & B which gives digitocxin, gitoxin; digitonin, gitonin	In Congestive Heart Failure, atrial fibrillation, etc
Thevetia (Trumpet flower, luck-nut tree	*Seeds of Thevetia peruviana **F:Apocynaceae***	Thevetin A, neriifolin, Cerebroside, Peruvoside,	Tincture is cathartic, emetic; cardiotonic
INDIAN SQUILL (Jangli pyaz,sea onion)	*Dries slices of leaves of Urginea indica F:**Liliaceae***	Scillaren A & B	Cardiotonic, stimulant, anticancer, emetic, asthma, expectorant,
Red Squill	*Red variety of European Squill*	Scilliroside & Scillirubroside	Rat poison
European Squill	*Dried slices of leaves of Urginea maritime*	Scillaren A, glucoscillaren A,	Cardiotonic, chronic bronchitis,

		Proscillaridin A	
STROPHANTHUS	*Seeds of Strophanthus kombe F:**Apocynaceae***	k-strophanthin, k-strophanthoside,	In cardiac failure,
Ouabain (G-Strophanthin)	*Strophanthus gratus or Acokanthera Schimperi*	Ouabain more potent than k-strophanthin	As above
SAPONIN GLYCOSIDES			
Dioscorea (Yam, Rheumatism root)	*Tubers of Dioscorea deltoidea **F:Dioscoreaceae***	Diosgenin, smilagenin, epismilagenin,	In Rheumatic arthritis
Safed Musali	*Tuberous roots of Chlorophytum orivillianum F:**Liliaceae***	Saponins, sapogenin (Hicogenin), Zn, Cu, P fibers	Aphrodisiac, tonic for debility
Liquorice (mulethi, Glycyrrhiza)	*Roots & stolon of Glycyrrhiza glabra F:**Leguminosae***	Glycyrrhizin (K & Ca salt) Flavonoids are liquiritin, isoliquiritin	Expectorant, demulcent, antispasmodic, peptic ulcer, arthritis
SHATAVARI (Shatmuli)	*Roots & leaves of Asparagus recemosus F:Lilianceae*	Shatavarin I-IV, Sarsapogenin, quercetin, rutin	Galactogogue, diuretic, anti oxytocic activity
Brahmi (Jalbrahmi)	*Leaves & stem of Bacopa moniera **F: Scrophulariace***	Brahmine, Herpestine; sapnins bacosides A &B	Nervine tonic, in asthma, epilepsy, anti cancer,in dementia
Momordica (Bitter Gourd, Karela)	*Fruits of Momordica charantia **F:Cucurbitaceae***	Charantin, momordicin, ascorbic acid	Stomachic, tonic, rheumatism,diabetes, gout
Brahmi (Mandukparni)	*Centella asiatica F:Umbellierea*	Asiaticoside, Madecassoside	Nervine tonic, sedative, spasmolytic, anti stress, skin diseases
Ginseng (Panax)	*Roots Panax ginseng F:**Araliaceae***	Ginsenosides, Panaxosides,	Immunomodulatory drug, aphrodisiac, demulcent, anemia
Senega (Radix, Rattlesnake root)	*Roots of Polygala senega F:**Polygalaceae***	Senegin, Polygalic acid	Expectorant, chronic bronchitis,
Quillia (Soap bark, Panama wood)	*Bark of Quillaja saponaria F:**Rosaceae***	Quillaic acid, quillaia sapotaxin	Expectorant, emulsifying agent, in prep of shampoos
Gokhru (Puncture vine)	*Fruits of Tribulus terrestris F:**Zygophyllaceae***	Steroidal saponins gitogenin, chlorogenin, ruscogenin. Flavonoids;	Diuretic, tonic, in calculous affection, in painul micturition, aphrodisiac, gout

		alkaloids:harmine	
CYANOGENETIC GLYCOSIDES			
Bitter almond (Amygdala amara)	*Ripe seeds of Prunus amygdalus* ***F:Rosaceae***	Amygdalin	Sedative, oil used in demulcent lotions
Wild Cherry Bark (Virginia prune)	*Bark of Prunus serotina* ***F:Rosaceae***	Prunasin, p-coumaric acid, benzoic acid	Expectorant
ISOTHIOCYNATE GLYCOSIDES			
Mustard	*Ripes seeds of Brassica nigra* ***F:Crucierae***	Sinigrin,	Condiment,emetic, counter irritant, rubefacient
FLAVANOL GLYCOSIDES			
SILYMARIN (Milk Thistle, Wild Artichoke	*Ripe seeds of Silybum marianum F:****Asteraceae***	Flavolignans Silybin, silycrystin, silydianin	In liver diseases,
GINGKO (Maiden hair tree, kew tree)	*Dried leaves of Gingko biloba F:****Gingkoaceae***	Ginkgetin, GingkolideB, isoginkgetin,gingkolic acid & bilobetin	Metabolic & vascular diseases; gingkolide B in sepsis, asthma,
Buck Wheat	*Fagopyrum esculentum F:****Polygonaceae***	Rutin (Hesperidin or Vitamin P)	Treat capillary bleeding, in retinal haemorrhage
COUMARIN & FURANOCOUMARIN GLYCOSIDES			
Tonka Bean	*Dried seeds of Dipteryx odorata* ***F:Leguminosae***	Coumarin	Flavoring agent
Visnaga (Khella, Picktooth fruit)	*Dried fruits of Ammi visnaga* ***F:Umbelliferae***	Khellin, visnagin, khelloside	Smooth muscle relaxant, coronary vasodilator, in asthma, whooping cough
AMMI	*Fruits of Ammi majus* ***F:Umbelliferae***	Bergapten, isopimpilin, xanthotoxin,	Increase melanin formation, idiopathic vitiligo,
Psoralea Fruit (Bavchi)	*Ripe fruits of Psoralea coryliolia* ***F:Leguminosae***	Psoralen, isopsoralidin, psoralidin	Leucoderma,leprosy, psoriasis,
Cantharides (Spanish flies,	*Dried insects (beetles) of Cantharis vesicatoria* ***F:Meloidae***	Cantharidin,	Irritant,vesicant, rubefacient. Hair growth stimulant
ALDEHYDE GLYCOSIDES			
Vanilla (Baunilha)	*Unripe fruits of Vanilla planifolia* ***F:Orchidaceae***	Vanillin, glucovanilic acid,	Flavoring agent

PHENOL GLYCOSIDES			
BEARBERRY (Uva ursi, Busserole)	*Dried leaves of Arctostaphylous uva-ursi* ***F:Ericaceae***	Arbutin, quercetin, ursone,	Diuretic,astringent, in urethritis, cystitis
STEROIDAL GLYCOALKALOIDS			
Solanum Khasianum	*Dried seeds of Solanum Khasianum* ***F:Solanaceae***	Solasodine, solakhasianin	It is precursor for synthesis of steroidal synthesis
GLYCOSIDAL BITTERS			
Gentian	*Fermented rhizomes & roots of Gentian lutea* ***F:Gentianaceae***	Gentiopicrin, Gentiopicroside, amarogentin, gentinin	Bitter tonic, appetizer
Picrorrhiza (Indian gentian, kutki)	*Dried rhizomes of Picrorrhiza kurroa* ***F:Scrophulariaceae***	Picroside I & II, Kutkoside,	Bitter tonic, febrifuge antiperiodic, laxative
Chirata (East Indian Balmony	*Entire herb of Swertia chirata* ***F:Gentianaceae***	Chiratin, amarogentin, gentiopicrin	In constipation, febrifuge, dyspepsia, in scanty urine, epilepsy
Quassia (Bitter wood, Jamaica quassia)	*Stem wood of Picrasma excelsa* ***F:Simarubaceae***	Quassin, neoquassin, picrasmin	Bitter tonic, as enema; in pediculosis;
Kalmegh (Kirayat, Andrographis)	*Dried leaves & tender shoots of Andrographis paniculata* ***F:Acanthaceae***	Andrographolides	Bitter tonic, hepatoprotective, anthelmintic, in dysentery, dyspepsia antityphoid,
Gymnema (Gudmar, Madhunashini)	*Leaves of Gymnema sylvestre* ***F:Asclepediaceae***	Pentriacontane, hentriacontane, gymnemic acid, betain,choline	Antidiabetic, diuretic, stomachic,
HENNA (Egyptian privet)	*Leaves of Lawsonia inermis* ***F:Lythraceae***	Lawsone,gallic acid, Hennosides A, B &C	In hair dye,

CHEMICAL TESTS:

Borntrager's Test for Anthraquinone (senna): Powder drug extracted with ether, filtered extract made alkaline by NH_3 or caustic soda, after shaking aqueous layer shows pink, red or violet color. (Anthranols show negative. Anthrones are detected with their fluorescence tests.

Chemical Test for Aloes:

- Boiled aloe powder and filtered. Bromine solution is added to filtrate which gives pale yellow precipitate.
- **Schoenteten's reaction**: Powdered filtrate is treated with Borax mix well, few drops of solution added to test tube nearly filled with water, a green fluorescence appears.

Special Test for different varieties of Aloes:

Nitrous Acid Test: Sodium nitrate with acetic acid added to aloe solution	Curacao aloe – pink to carmine color Cape aloes – faint pink color Socotrine & Zanzibar – less color change
Nitric Acid Test: add HNO3 to aqueous drug	Curacao aloes – deep brownish red color Cape – brownish color change to green Socotrine – pale brownish-yellow color Zanziber – yellowish brown color
Cupraloin Test: aqueous solu of Aloe, a drop of CuSO4 added, followed by NaCl +alcohol (Klunge's isobarbaloin)	Curacao – wine red color after 4 hours Cape aloes – faint color change to yellow Zanzibar, Socotrine – No color
Modified Anthraquinone Test: aloe solution is treated with FeCl3+HCl, added ether/CCl4, organic layer separated & shaken with dil NH3	Ammonical layer shows rose-pink to cherry red color **(this test For c-glycosides**)

RHUBARB:

- Positive test for Modified Anthraquinone test
- To rhubarb solution, add alkalies, shows red color due to anthraquinone.

DIGITALIS:

Keller Kiliani Test for Digitoxose:	Reddish brown layer acquires bluish-green color
Legal Test: extract is dissolved in pyridine, Sod nitroprusside solution added	Alkaline pink/red color produced

Baljet Test:to section of digitalis, sodium picrate solution added	Yellow to orange color

Indian Squill:

- Mesophyll stain with alkaline colarin solution red color appears
- Mesophyll stain with 0.1 M Iodine solution gives reddish purple color.

STROPHANTHUS:

- Addition of H2SO4 to glycoside, shows green color.

SAFED MUSALI:

- Drug, on addition of H2SO4,shows deep yellow color.

Wild Cherry Bark:

- Small pieces of Bark put in flask containing water. A filter paper soaked in sodium picrate solution and suspend at flask neck. Yellow color of paper change to brick red due to liberated hydrocyanic acid.

MICROSCOPIC STUDIES:

Senna Leaves	Epidermis shows presence of unicellular, thick-warty trichomes. Rubiaceous/Paracytic stomata. Palisade tissue enclosing cluster crystals of calcium oxalate.

	Indian Senna	**Alexandrian Senna**
Vein islet Number	19.5-22.5	25-29.5
Stomatal Index	17 to 20	11.4-13.3
Palisade Ratio	7.5 (upper epidermis 5.2 (Lower)	9.5 (upper) 7.0 (lower)

Curacao Aloes	Fragments consisting of large number of very small needles or slender prisms.
Cape Aloes	Transparent, brown, angular or irregular fragments
Socotrine Aloes	Fragments consist of quite large prisms either present in group or in dispersed form
Zanziar aloes	Irregular lumps in which modular masses are emedded.

Cascara Bark: Transverse section shows cork, cortex, sclereids, primary & secondary phloem. Cortex composed of collenchyma externally, cellulosic parenchyma inner side which contains large number of Calcium oxalate crystals. Many cells of phloem & Parenchyma contain prisms of calcium oxalate,form a crystal sheath to each group of phloem fibres.

DIGITALIS LEAVES	Digitalis is dorsiventral leaf contain Anomocytic stomata on both surfaces. Trichomes are uniseriate,multicellular, bluntly pointed.; Glandular & collapsed cell trichomes. No Calcium oxalate crystals & sclerenchyma. Collenchyma present in 3 different places upper & lower dermis & pericyclic part.

INDIAN SQUILL:	Transverse section shows polygonal axially elongated epidermis, parenchymatous mucilaginous mesophyll with raphides of Calcium oxalate crystals and is interrupted by small vascular bundles.
European Squill	As above
Red Squill	Anthocyanin pigment present in mesophyll cells.

Dioscorea Tubers: Epidermis absent, Endodermis & Pericycle are indistinguishable.

Liquorice Stolon: Unpeeled drug shows presence of polyhedral tubular brownish cork cells. Fibres are thick, lignified or partially lignified, in the group of 10-15 in phloem and xylem. Starch & calcium oxalate crystals are present in parenchyma. Root is characterized by tetrarch xylem & absence of pith.

Gentian Root: Rhizome shows pith, but root don't. cortex has parenchyma with oil globules and calcium oxalate. Phleom present but phloem fibers absent. Drug does not contain sclereids.

Picrorrhiza Rhizome: Periderm constitute 8-10 layers of thin walled cork. Pith consists of thick parenchymatous cells.

Quassia Wood: Contains large xylem vessels with bordered pits. Wood fibers are thick walled with pointed ends, medullary rays are bi or multiseriate. Wood parenchyma appears in irregular concentric rings.

ADULTERANTS & SUBSTITUTES

Drug	Adulterant/Substitute
Tinnevelly Senna	Dog Senna (C obovata), Palthe senna (C auriculata), Bombay, Mecca Senna. Dog senna leaves show papillose cells in lower epidermis. Palthea senna lealets show long hair shows crimson color when boiled with chloral hydrate solution.
Aloe	Natal Aloe (resembles with Cape alow) as substitute. Mocha Aloe: brittle lack & glassy aloes with strong odor
Cascara	R. californica, R. fallax and frangular bark are substitutes. Frangula bark has uniform coat of lichens & wider medullary rays
Digitalis	Verbascum Thapsus (branched candelabra trichomes) Primerose (Primula) leaves (uniseriate covering trichomes) Comfrey (Symphytum) leaves contain multicellular trichomes forming hook at the top
Indian Squill	Scilla hyacintoiana
Dioscorea	Costus speciosus substitute
Liquorice	Manchurian (G uralensis) Russian (G glabra variety glandulifera)
Cantharis	Chinese cantharis (Mylabris cichorii/pustulata)
Chirata	S densifolia, S ciliate,S paniculata
Kalmegh	Andrographis echioides substitute

Fluorescence Tests:

- Indian Rhubarb shows Deep Violet fluorescence in UV Light
- Rhapnotric Rhubarb shows Blue fluorescence in UV Light.
- Hypericum contain Hypericin, a Red Fluorescent pigment.
- Small quantity of psoralea drug dissolved in alcohol, add 3 times of propylene glycol+5 times of acetic acid+40 times of water, A Blue Fluorescence observed under UV Light.
- Quassia shows Blue Fluorescence in acidified alcohol.

TANNINS

Tannins are mixtures of complex organic compounds in which polyphenols are present, generally with o-dihydroxy or o-trihydroxy group on a phenyl ring. Tannins are secondary metabolites present in cell sap & vacuoles.

CHEMICAL TESTS:

- Solution of Tannin precipitates Gelatin, Alkaloids.
- Tannins are precipitated by salts of Cu, Tin and Lead.
- Tannins are precipitated by strong Potassium Dichromate or chromic acid solution
- Tannins with $FeCl_3$ give bluish-black/brownish green color.
- Tannins with Potassium Ferricyanide with NH_3 give deep red color.
- Tannins are precipitated by 2% solution of phenazone.

Goldbeater's Skin Test: Membrane of intestine of ox is treated with HCl, rinsed with distilled water and place in tannin solution followed by washing with distilled water and put in $FeSO_4$ solution. Brown/Black color is developed.

Hydrolysable Tannins: These tannins are hydrolysale y acids or enzymes & products of hydrolysis are gallic acid/ellagic acid. On dry distillation converted to pyrogallol. These tannins produce Blue color when treat with FeCl3 solution. Ex: nutgall, rhubarb, clove & Chestnut, Myrobalans, pomegranate bark.

Condensed Tannins (Proanthocyanidins): These are non-hydrolysable tannins, related to flavonoid pigment. On dry distillation gives catechol. Tannins with $FeCl_3$ gives brownish-green color. Ex: male fern rhizome, cocoa, cola, areca seeds, black catechu etc.

Pseudotannins: They do not obey Goldbeater's skin test. Ex Chlorogenic acid in coffee, nuxvomica; ipecacuanhic acid in ipecacuanha; catechins in cocoa.

HYDROLYSABLE TANNINS			
Drug	**Biological Source**	**Chemical constituent**	**Uses**
Myrobalan (Harda, Haritaki)	Dried fruits of Terminalia chebula F:**Combretaceae**	Chebulic acid, chebulagic acid, gallic acid	Astringent, stomachic, in triphala churna
Bahera (Bibhitak)	Dried fruits of T. belerica	Gallic acid, chebulagic acid	Astringent, in triphala churna
Arjuna	Stem bark of Terminalia arjuna	Ellagic acid, β-sitosterol	Cardiotonic, hypotensive
Tannic Acid	Fermented oak galls of Quercus infectoria F:**Fagaceae**	Gallic acid & Glucose	Astringent, in sore throat, in piles; Antidote in alkaloid, heavy metal poisoning
Amla (Indian Goose berry)	Fruits of Emblica officinalis **F:Euphorbiacee**	Vitamin C, Phyllemblin,	Diuretic,dysentry, in Triphala & Chyavanprash, antioxidant,
CONDENSED TANNINS			
Ashoka Bark	Stem of Saraca indica F:Leguminosae	Catechol, Ketosterol	Uterine tonic, oxytocic, menorrhagia
Black/Khdir Catechu (cutch)	Heartwood of Acacia Catechu F:Leguminosae	Acacatechin, quercetin	Astringent for boils, skin eruptions

Pale Catechu (Gambier)	Leaves & young shoots of Uncaria gambier F:Rubiaceae	Catechin, catechutanic acid	Astringent in treatment of diarrhea
Pterocarpus (Malbar kino, Bijasal)	Dried juice of plant Pterocarpus marsupium F:Leguminosae	Kinotannic acid, kinored, k-pyrocatechin	Hypoglycemic, astringent, dysentery, in diabetes, toothache

ADULTERANTS:

Arjuna	Terminalia tomentosa. (Extract of arjuna gives pinkish fluorescence, while T tomentosa gives pale blue.

CHEMICAL TESTS:

BLACK CATECHU:

- Black catechu + vanillin + HCl → Black Catechu
- Catechin + HCl → Phloroglucinol, burn with lignin gives purple/magenta color. For this test, tannin extract is taken on match stick dipped in HCl and heated near the flame shows above color.
- Lime water added to aqueous extract of Black catechu gives Brown color, which turns to red precipitate.
- Dilute solution of Black catechu + Ferric ammonium sulphate → Green color

PALE CATECHU:

- It gives test for catechin (Match stick test)

- Drug is extracted with alcohol and NaOH is added. Followed by addition of light petroleum. Mix is shaken, ***Green Fluroscence*** observed in light petroleum layer. (Distinction from black catechu)
- Drug is warmed with CHCl3 and filtered in porcelain dish and evaporated to dryness. Due to presence of chlorophyll, it shows Greenish Yellow color.

PTEROCARPUS:

- Drug solution is treated with $FeSO_4$, green color is produced.
- With alkali, violet color is produced.
- With mineral acid, a precipitate is obtained.

LIPIDS

Lipids are the substances of animal or plant origin and comprise of fixed oils, fats and waxes. Fatty acids are reserved food materials of plants & animals.

- Those which are liquid at 15.5-16.5° are called fixed oils, while those which are solid or semi-solid at above temperature are termed as fats.

Properties of Fatty Oils:

- They are non-volatile & cannot be distilled.
- They do have food value and can be saponified.

Fats &Y Oils are esters of glycerol which have 4-24 carbon atoms. These fatty acids may be saturated, monounsaturated or polyunsaturated.

Essential Fatty Acids: The unsaturated fatty acids like lenoleic acid, linolenic acid & arachidonic acid, as they are not produced in the body and required in the diet.

CHEMICAL TESTS:

- **NaOH**: 1 ml 1% CuSO4 + fixed oil + NaOH → Blue solution obtained
- **$NaHSO_4$**: fixed oil + NaHSO4→ Pungent odor indicating glycerine is present.

Classification Of Fixed Oils:

Oils & Fats (**Vegetables**)	Fats	Cocoa Butter, Kokum Butter, Nutmeg butter, coconut oil, Palm Oil, Mango kernel oil
	Non-drying oils	Olive oil, Peanut oil, Almond oil, Croton oil, Rice-bran oil
	Semi-drying Oils	Castor oil, Mustard oil, sesame oil, Rapeseed oil, cottonseed oil, safflower oil
	Drying Oils	Linseed oil, Poppy seed oil, Hemp oil, Walnut oil
Animal Oils & Fats	Marine animals	Fats – Bone tallow Oils – Cod liver oil, Shark liver oil
	Terrestrial animals	Fats – Lard, Mutton-tallow, Butter suet Oils – Lard Oil, Neat-foot oil

Drug	Biological Source	Chemical constituent	Uses
Arachis oil (Peanut oil)	Arachis hypogaea F:Leguminosae	Glycerides of oleic, linoleic & Palmitic acids	Solvent for IM injections, in liniments, soaps
Castor Oil (ricinus oil)	Ricinus communis F: Euphorbiaceae	Triglycerides of ricinoleic acid, linoleic, stearinc acids	Cathartic, in soaps,
Olive Oil	Olea europoea F:Oleaceae	Triglycerides of olein, palmitin, linolein	Emollient, soothing agent for inflammed skin
Chaulmoogra Oil (Hydnocarpus oil)	Seeds of Taraktogenos kurzhii, H anthelmintic F:Flacourtriaceae	Chaulmoogric acid, hydnocarpic acid, palmitic acid	Bactericidal in TB, Leprosy, psoriasis, Rheumatism
LINSEED	Linum Usitassimum F:Linaceae	Mucilage, cyanogentic glycoside Linamarin	Demulcent, used as poultice
Linseed Oil	Seeds of Linus Usitatissimum	Glycerides of palmitic, stearing, oleic, linoleic & linolenic acid, sterol	Lotions, liniments; used in treatment scaies & other skin diseases, emollient
Sesame Oil (Teel Oil, Gingelly oil, Benne oil)	Sesamum indicum F:Pedaliaceae	Glycerides of oleic, linoleic,stearic, arachidic oil; lignans	Laxative, demulcent, emollient; as vehicle for IM injections

		sesamin & sesamolin	
Kokum Butter (Goa butter, Mangosteen oil)	Garcinia indica F:Guttierae	Glycerides of stearic, oleic, palmitic, linoleic acids	Demulcent, emollient, astringent; in ointments, suppositories
Safflower Oil	Carthamus tinctorius F:Compositae	Glycerides of palmitic, stearic, arachidic,oleic, linoleic acids	Dietary supplement for hypercholestermia & in atherosclerosis
Corn Oil (Maize oil, Mazola Oil)	Zea Mays F:Graminae	Glycerides of linoleic, linolenic,oleic,palmitic acids, Tocopherol (Vit E),Uiquinone	High calorie dietary supplement; lowers blood cholesterol;
Rice Bran Oil	Husk of paddy & endosperm of seeds of Oryza sativa F:Graminae	20-25% saturated & 80-85% Unsaturated FA, oleic, linoleic, palmitic acids; Squalene, Vitamin E	Antioxidant,in cosmetics, emollient
Black Mustard Oil (Sarson ka tel)	Brassica nigra F:Cruciferae	Glycerides of arachidic, behenic, eicosenoic, linolenic, oleic,myristic; sinigrin	Local irritant & emetic dut to allyl isothiocynate, vesicant, rubefacient,
Poppy Seed Oil	Dried seeds of Papaver somniferum F:Papaverace	Linoleic acid,Palmitic, arachidic, Oleic acids	Used in varnishes, soaps, paints
Karanja Oil	Pongamia glabra F:Papillionaceae	Lignoceric, palmitic, oleic acid,linolenic, stearic,arachidic acid; karanjin	Used in scabies, herpes, leucoderma, cutaneous diseases
Neem oil (Margosa oil)	Azadirachta indica F:Meliaceae	Glycerides of saturated & unsaturated FA, S containing compounds nimbin, nimbinin, nimbidol, nimbidin	Nimbin, Nimbidin have anti viral properties. In rheumatism, pesticide,
Cotton seed oil	Gossypium herbacium F: Malvaceae	Triglycerides of fatty acids, palmitic,oleic & Linoleic acids	In cosmetics, emollients, employed as pediculicide,
Gossypol	Gossypium herbaceum F:Malvaceae	Gossypol pigment	Spermicidal, antiviral, antiprotozoal, anti tumor
Cocoa Butter (Theobroma oil, cocoa butter)	Seeds of Theobroma cacao F:Sterculiaceae	Glycerides of stearic, palmitic, oleic, arachidic & Linoleic acids	Base for suppositories & Ointments

Shark Liver Oil (Oleum selachoids)	Shark liver of Hypoprion brevirostris & Galeorhinus zyopterus, scoliodon, carcharias	Vitamin A,	Antixeropthalmic factor,
Cod Liver Oil (Oleum morrhi)	Liver of cod fish Gadus morrhua F:Gadidae	Vitamin A & D; glyceryl esters of oleic, linoleic, gadoleic, myristic, palmitic acids.	Nutritive, Rickets, TB; cholesterol lowering property
Hydrous Wool Fat (Lanolin, Adeps Lanae)	Wool of sheep Ovis aries F:Bovidae	Esters of cholesterol, isocholesterol with carnaubic, oleic, myristic, lanoceric, lanopalmiticacid.	Lanolin used in water absorbable ointment base; allergic
Yellow Bees Wax (cera-flava)	Honey comb of Apis melliferae F:Apidae	Esters of monohydric alcohols, myricin, melissic acid	In ointments (hardening), plasters & polishes, lip stics, Praffin Ointment IP
Carnauba Wax (Brazil wax)	Copernica pruniera leaves F:Palmae	Esters of hydroxylated FA ie. Carnaubic & cerotic acid	Cosmetics, tablet coating, deplilatories, deodorants;
Suet (Sevum, Mutton Suet)	Internal fat of abdomen of sheep Ovis aries F:Bovidae	Palmitin & stearin & olein	In ointment base
Lard (Adeps)	Fat obtained from abdomen of hog Sus scrofa F:Suidae	Olein, stearing & Palmitins	Used as an ointment base, in formulations; benzoin resin as preservative
Spermaceti (Cetaceum, Spermawax)	Sperm whale of Physester macrocephalus F:physeteridae	Cetyl palmitate, free cetyl alcohol & esters of lauric, myristic & stearic acids	Used as emollient & in preparation of ointments, in cold creams.
Wheat Germ Oil	Triticum aestivum F:Graminae	Linoleic acid, linolenic acid,oleic acid, Vitamin E	Nutritional supplement;
Jojoba Oil	Mix of liquid wax ester of Simmondsia chinensis F:Buxaceae	Oil is not triglyceride, mix of long chain esters MUFA	In cosmetics, lubricant, substitute for sperm whale oil
Lecithin (Vitellin, Phosphatidyl choline)	Soybean oil, egg-yolk, corn	Glycerol, FA, phosphoric acid and choline	Imp in transmission of nervous impulses, antioxidant,
Evening Primrose Oil (King's cureall)	Oenothera biennis F:Onagraceae	Linoleic acid,Gamma Linolenic acid.	Dietary supplement, Prostaglandin precursor, in premenstrual syndrome, MS

ADULTERANTS:

Peanut Oil	*Cotton seed oil*: oil + alcohol + CS_2 → Pink/red color indicate cotton seed oil (Halphen's test) *Sesame oil*: oil + HCl + sucrose → Pink color indicate sesame oil(Baudouin's test)
Linseed oil	*Cotton seed oil, mineral oil, sunflower oil*
Cocoa Butter	*Mango kernel oil,*
Yellow Bees Wax	*Colophony, hard paraffin, stearic acid, Japan wax, spermaceti, carnauba wax*
Mustard Oil	*Argemone oil*

ANALYTICAL PARAMETERS FOR OILS & FATS:

Iodine Value: The weight of iodine absorbed y 100 parts by weight of the sample of fat or oil. It is measure of extent of unsaturation. Higher the value, higher susceptibility to rancidity.

Saponification Value: No of milligrams of KOH required to neutralize the fatty acids resulting from complete hydrolysis of 1 gm of sample of oil/fat. Saponification value is inversely proportional to avg molecular weights of fatty acids present in the oil.

Hydroxyl Value: No of milligrams of KOH required to neutralize the acetic acid capable of combining by acetylation with 1 gm of fat/oil.

Acetyl Value: No of milligrams of KOH required to neutralize acetic acid capable of combining by acetylation with 1 gm sample of fat/oil.

Polenski Value: No of N/10 KOH solution required to neutralize water-insoluble, steam distillable acids liberated by hydrolysis of 5gm of fat.

ENZYMES

DRUG NAME	Biological Source	Uses
Diastase (Amylase)	From salivary diastase, pancreatic salivary or malt diastase (Amylolytic agent)	Digestant, in fermentation & brewing industry
Pepsin	Fresh stomach hog Sus scrofa F:Suidae; (proteolytic)	Max activity at pH 1.8; pepsin degrades proteins into peptones & proteoses
RENIN	Stomach of calf Bos Taurus F:Bovidae	Proteolytic; to prepare junkets & cheese
Pancreatin	Pancreas of Hog,Ox ; contains amylase,protease, lipase	In pancreatitis, fibrocystic diseases of pancreas
Pancrealipase	Pancreas of Hog; contains more lipase;	In chronic pancreatitis, cystic fibrosis
Trypsin	Pancreas of ox; Proteolytic;	Proteolysis of blood clot, necrotic tissue, purulent exudates; not act on living tissue
Chymotrypsin	Pancreas of ox; Proteolytic	Reduce soft tissue inflammation; in ophthalmology for dissection of zonule of lens for cataract extraction
Hyaluronidase	Sterile preparation from mammalian testes & semen	In injections to increase absorption rate
Muramidase	Present in tears, lungs, serum, leucocytes; (Mucolytic)	In bacterial & viral infections
Urokinase	Obtained from kidney;	Used to dissolve fibrin or blood clots in anterior chamber of eye & in pulmonary emboli
Fibrinolysin	Activation of human plasminogen (Proteolytic)	In treatment of thrombolytic disorders
Streptokinase	From Streptococci group C,	Activates plasminogen to plasmin
Collagenase	Fermentation of Clostridium histolyticum	In debridement of dermal ulcers, burns & other necrotic lesions
Sutilains	From Bacillus subtilis; Proteolytic	In burns, incisional traumatic & pyrogenic wounds & ulcers
L-Aspraginase	From E. Coli;	In acute lymphocytic leukemia; AL lymphoma; immuno-suppressive

Bromelain	Mix of proteolytic enzymes from Pineapple (Ananas Comosus F:Bromeliaceae	In soft tissue inflammation; oedema due to surgery & injury
Papain	Unripe fruit of Carica Papaya F:Caricaceae (Proteolytic)	Anti-inflammatory agent, reliving symptoms of episiotomy;
Serratiopeptidase	From bacteria Serratia species present in silk worm gut; proteolytic,	In inflammation; sputum liquification; increase antibiotic effects

VOLATILE OILS

Volatile Oils – Odorous, volatile principles of plant & animal sources

Ethereal Oils – Oils that evaporates when exposed to air at ordinary temperature

- **Volatile oils** are derived from *terpenes* and their oxygenated compounds (*terpenoids*). They are made up of isoprene units (C_5H_8). See below ex:
- Volatile oils are soluble in alcohol, ether & lipid solvents & insoluble in H_2O.
- They are optically active and high refractive index.

Volatile Oil	Terpenoid
Caraway Oil	Carvone, limonene
Citronella oil	Geraniol, citronellal, farnesol
Eucalyptus oil	Cineole
Geranium oil	Geraniol

Volatile Oil extraction Methods:

i)Hydro-distillation: Comprising water distillation, water & steam distillation for volatile oil extraction.

ii)Enfleurage: Used for extraction of delicate perfumes.

iii)Ecuelle: Used for extraction of citrus oils.

Alcohol volatile Oils	Peppermint, cardamom, coriander, orange flower oil, rose oil, sandalwood oil

Aldehyde volatile oil	Cinnamon, lemon peel, orange peel, citronella oil, lemon grass, bitter almond
Ester Volatile Oils	Gaultheria, Lavender, Mustard
Hydrocarbon volatile oils	Turpentine, Black pepper, Hops
Ketone volatile oils	Caraway, Spearmint, buchu, camphor, must, civet oil
Oxide volatile oils	Chenopodium, eucalyptus
Phenolic ether	Anise, Fennel, Nutmeg
Phenol volatile oils	Clove, Thyme, Creosote

Name of Terpenoid	**No of isoprene Units**	**Molecular Formula**
Hemiterpene or isoprene	1	C_5H_8
Monoterpenes	2	$C_{10}H_{16}$
Sesquiterpenes	3	$C_{15}H_{24}$
Diterpenes	4	$C_{20}H_{32}$
Triterpenes	5	$C_{30}H_{48}$
Tetraterpenes or Carotenoids	6	$C_{40}H_{64}$
Pentaterpenes	7	$C_{50}H_{80}$
Polyterpenes	N	$(C_5H8)_n$

MONOTERPENOIDS			
Drug name	**Biological source**	**Chemical constituent**	**Uses**
Camphor Oil	Wood of Cinnamomum camphora F:Lauraceae	Safrole, dipentene, camphor, eugenol	Rubefacient, counter irritant, in soaps, tooth powders
Chenopodium oil (American wormseed oil)	Flower & fruits of Chenopodium ambrosiodes F:Chenopodiaceae	Ascaridole, p-cymene, myrcene	Anthelmintic, against roundworms, hookworms
Eucalyptus oil (Dinkum oil)	Leaves of Eucalyptus globules F:Myrtaceae	Cineole (Eucalyptol), pinene,	Counter irritant, antiseptic, expectorant, as nasal drops
Geranium Oil	Leaves of Pelargonium graveolens F:Geraniaceae	Geranium oil contains alcohols (β-citronellal,	Flavoring agent,

		geraniol),esters geranyl acetate, tiglate	
Lemon Grass Oil (Indian Melissa oil	Leaves & aerial parts of Cymbopogon flexuosus F:Graminae	Citral, methylheptenol, nerol,	Flavoring agent,
Turpetine Oil	Pinus roxburghii, p.palustris F:Pinaceae	α-pinene, β-pinene, camphene, β-phellandrene	Counter irritant, rubefacient, in chronic bronchitis
Peppermint oil (Mentha oil)	Fresh flowering tops of Mentha piperita F:Labiatae	l-menthol, menthone, menthofurone; pulgeone,	Carminative, stimulant, flavoring agent, spasmolytic, smooth muscle relaxant,
SPEARMINT (mint)	Dried leaves & flowering tops of Mentha spicata F:Laiatae	l-carvone, linalool, pinene,cineole	Carminative, flavor in tooth paste, mouth washes
Caraway (carum, caraway seed)	Ripe fruit of carum carvi F:Umbelliferae	Carvone,limonene, dihydrocarvone,	Aromatic, stimulant, carminative
Cardamom	Dried ripe fruits of Elettaria cardamomum F:Zingiberaceae	Cineole, terpinyl acetate, terpineol, terpinene	Aromatic, stimulant, carminative,
Coriander	Ripe fruit of Coriandrum sativum F:Umbelliferae	D-linalool, l-borneol, geraniol, pinene	Aromatic, stimulant, flavoring agent, in griping
Ajowan	Dried ripe fruit of Trychyspermum ammi F:Umbelliferae	Thymol, p-cymene, terpinene,	Antispasmodic, stimulant, carminative, sore throat,
Dill (Anethum, European dill)	Ripe fruit of Anethum graveolens F:Umbelliferae	Carvone, d-limonene, phellandrene	Aromatic, gripe water, stimulant, carminative,
Fennel	Dried ripe fruits of Foeniculum vulgare F:Umbelliferae	Fenchone (ketone) Phenolic ether anethole	Carminative, aromatic, stimulant, expectorant
Lemon Peel	Pericarp of fruit of Citrus limonis F:Rutaceae	Limonene, geranyl acetate, terpineol, Hesperidin, pectin,	Carminative, stimulant, flavoring agent
Bitter Orange Peel	Peel of pericarp of C. auranticum F:Rutaceae	Limonene, vitamin C, hesperidin, pectin,	Stomachic, aromatic, carminative

Nutmeg (Myristica)	Dried kernels of Myristica fragrans F:Myristicaceae	Myristicin, elimicin, saffrole,	Aromatic, stimulant, carminative, flavoring agent
Cassia Cinnamon	Stem bark of Cinnamomum cassia F:Lauraceae	Cassia oil contains mucilage, starch, cinnamic aldehyde, eugenol, cinnamyl acetate	Carminative, stimulant, flavoring agent, aromatic.
Cinnamon (Kalmi-Dalchini)	Dried inner bark of shoots of Cinnamomum zeylanicum F:Lauraceae	Cinnamaldehyde, eugenol, benzaldehyde, phellandrene, cymene, caryophyllene etc	Carminative, stomachic, astringent, flavoring agent,
Jatamansi (Nard)	Dried rhizomes of Nardostachys jatamansi F:Valerianaceae	Jatamansic acid, jatamansone, nardostachone	Sedative, diuretic, emmenagogue, stomachic; in epilepsy,hysteria
Rasna (Galanga, East Indian root)	Rhizomes of Alpinia officinarum F:Zinziberace	Methyl cinnamate, cinole, camphor, pinene, galangol, alpinol,	Aromatic, stimulant, carminative, in rheumatism
Garlic (Allium)	Bulbs of Allium sativum F:Liliaceae	Allyl propyl disulphine, allin, allicin; contains Fe, P & Cu	Aphrodisiac, expectorant, in pulmonary condition, anthelmintic, rubeacient, in high BP, atherosclerosis
Tulsi (Holy basil, Sacred basil)	Ocimum sanctum F:Labiatae	Eugenol, carvacrol, caryophyllin	Antibacterial, insecticidal, aromatic, spasmolytic
Benafsha (Sweet violet)	Dried aerial parts of Viola odorata F:Violaceae	Violin, rutin & cyanin,	Expectorant, antipyretic, in eczerma,
Kapur Kachari (Spiked ginger lily	Rhizomes of Hedychium spicatum F:Zingiberaceae	Paramethoxy cinnamic acid ester, cineole limonene, ethyl cinnamate	Stomachic, stimulant, tonic, carminative
Black Pepper	Fruit of Piper nigrum F:Piperaceae	Piperine (alkaloid); l-phellandrene, caryophyllene	Stimulant, stomachic, carminative

Oil of Vetiver (Khus oil)	Roots of Vetiveria zizaniodes F:Graminae	Vetivenol, vetiverol, α & β – vetivones; Indian var contain khusal, khusitol	Stimulant, refrigerant, in prickly heat powder
Rosemary Oil	Flowering tops of Rosmarinus officinalis F:Labiatae	Borneol, Bornyl acetate, camphor, eucalyptol, pinene,	Rubefacient, flavoring agent, hair lotions,
ANISE (anise fruit, aniseed)	Ripe fruit of Pimpinella anisum F:Umbelliferae	Anethol; methylchavicol; anisaldehyde	Stimulant, carminative, condiment
Cummin (Jira)	Ripe fruit of Cuminum cyminum F:Umbelliferae	Cuminaldehyde, α, β-pinene, cuminic alcohol	Stimulant, carminative, diarrhea, dyspepsia
Celery (Apium)	Fruit of Apium graveolens F:Umbelliferae	d-limonene, sedanoic acid, sedanolide, d-selinine	Stimulant, nervine sedative & tonic, rheumatism
Lavender oil	Flowering tops of Lavandula officinalis F:Labiatae	Linalyl acetate, Linalool, pinene, geraniol	Stomachic, carminative, in cosmetics
Gaultheria Oil (Betula oil, oil of wintergreen, sweet birch oil)	Leaves of Gaultheria procumbens F:Ericaceae	Methyl salicylate, enanthic alcohol; Gaultherin	Counter irritant, rheumatism; against hookworm In Perfumery
Oil of Palmarosa (Rosha oil, Geranium oil)	Leaves of Cymbopogon martini F:Graminae	Geraniol, citronellal dipentene, Linalool	In perfumes, cosmetics, skin diseases, rheumatism
Oil of citronella	Leaves of cymbopogon nardus F:Graminae	Geraniol, citronellal, d-camphene, limonene.	In perfumes, in mosquito repellent, flavoring agent
Musk (Moschus, Kasturi)	Perputial of musk deer Moschus moschierus F:Cervidae	Muskone	In perfume,
Civet (Zibeth)	Scent glands in external generative organs of civet cat Viverra zibetha F:Viverridae	Civetone, civetol, ethylamine,	Flavoring agent, in perfumery
Castoreum (castor, Canadian beaver)	Perpetual follicles of beaver Castor faber F:Castoridae	Castorin, benzyl alcohol	Flavoring agent,

Thyme (garden thyme)	Flowering tops of Thymus vulgaris F:Labiatae	Thymol, carvacrol, terpineol, Linalool	Expectorant, antispasmodic, anthelmintic

SESQUITERPENOIDS:

Artemisia (Worm seeds, Santonica)	Flower heads of Artemisia cina F:Compositae	Santonin (lactone), artemisin; cineole, pinene	Anthelmintic (Round worms);
Arteisinin	Artemisia annua (Chinese)	Artemisinin (Artemether developed by CDRI)	Antimalarial (Schizonticidal); most active in cerebral malaria
Davana Oil	Flowering herb of Artemisia pallens F:Compositae	Davanone, artemone,	Perfume, flavoring agent,
Arnica (Leopard's bane,Mountain tobacco, Wolf's bare)	Flower heads of Arnica Montana F:Compositae	Helenanolides (Helenalin, Arniolin, epoxyhelanli, Arnicin,	Tincture is used as counter irritant, in cosmetics,
Oil of Sandal wood (East Indian sandal wood)	Heart wood of Santalum album F:Santalaceae	α-,β-santalol; aldehyde santalal	Dysurea, in frequency of micturition, in TB of bladder; incense sticks
Clove (Caryophyllum,	Flower buds of Eugenia caryophyllus F:Myrtaceae	Eugenol, eugenol acetate, eugenin	Dental analgesic, carminative, flavoring agent, antiseptic,
Hops	Female flowers of Humulus lupulus F:Cannabinaceae	Humulone, cohumulone, lupulone,	Sedative, spasolytic, in IBS,
Saussurea (Costus, kuth)	Dried roots of Saussurea lappa F:Compositae	Saussurine, kusthin, costuslactone,	In bronchial asthma, expectorant, antiseptic against streptococci
Acorus (Calamus, Ghoda vaj, Vaj)	Rhizome of Acorus calamus F:Araceae	Asaraldehyde, asarone, eugenol, Acorine	Carminative, vermifuge, in epilepsy, depression
Cubeb (Kaabchini, tailed pepper)	Unripe fruits of Piper cubeba F:Piperaceae	Cubebin, cubebic acid,	Stimulant, aromatic, in cough, urinary antiseptic
Valerian	Rhizomes, stolon of Valeriana wallichi F:Valerianaceae	Chatinine, valerine, borneol formate, camphene,	Antispasmodic, depressant, stimulant,

Feverfew (featherew, altamisia, pyrethrum)	Dried leaves of Tanacetum parthenium F:Compositae	Chrysanthemin A &B, parthenolide, borneol, farnesene,	In migraine, vertigo, arthritis, fever & menstrual disorders

DITERPENOIDS:

Taxus (Yew, Talispatra)	Taxus baccata, Taxus cuspidate F:Taxaceae	Taxol, cephalomannine, 10-deacetyl baccatin	Anticancer (targets on microtubules)
Forskolin	Roots of Coleus forskohii F:Laiatae	Coleon E (methylenequinone), barbatusin & Coleon F	Vasodilator, cardiostimulant effects; lower BP & IOT
TRITERPENOID			
AMBERGRIS	Sperm whale of Physester catodon **F:Physesteridae**	Amrein, Epicoprostanol & coprostanone	In perfumery
TETRATERPENOIDS & CAROTENOIDS			
Annatto (Arnotta, Annotta)	Dried seeds of Bixa orellana **F:Bixaceae**	Bixin (yellow Pigment) Isobixin, nor bixin,	Coloring agent,
Crocus (Saffron, Kesar)	Dried stigmas & upper part of styles of Crocus sativus **F:Iridaceae**	Crocin, crocetin, picrocrocin,	Coloring & Flavoring agent; antispasmodic,

RESINS & RESIN COMBINATIONS

Resins are mixture of essential oils, oxygenated products of terpenes & carboxylic acids. They are insoluble in water but soluble in alcohol, and non-polar organic solvents.

Drug	**Biological Source**	**Chemical Constituent**	**Uses**
Ginger (Zingiber)	Rhizomes of Zingiber officinale F:Zingiberaceae	α-Zingiberene, β-bisabolene, α-farnesene,	Stomachic, aromatic, carminative carminative, in motion sickness,
Ginger oleo-resin	As above	Zingerone, Gingerol, shogaol,	Flavor for carbonated beverages
Capsicum	Dried ripe fruits of	Capsaicin, capsanthin,	Carminative,

(chillies)	Capsicum annum F:Solanaceae	carotene, thiamine	appetizer, counter irritant, neuralgia, lumbago
Capsicum Oleo Resin	Capsicum extract by alcohol/acetone	Capsanthin,	Irritant, caminative,
Turmeric (Indian Saffron, Curcuma)	Rhizomes of Curcuma longa F:Zingiberaceae	Curcuminoids, curcumin; zingiberene, α,β-curcumenes	Condiment, coloring agent, antiinflammatoy,
Asafoetida (Devil's dung)	Rhizome, roots of Ferula foetida F:Umbelliferae	Asaresinotannol; ferulic acid, umbellic acid, umbelliferone	Nervine stimulant, intestinal flatulence, flavoring agent
Cannabis (Ganja, Marihuana, Indian Hemp)	Flowering tops of female plant Cannabis sativa F:Cannabinaceae	1,3,4-trans tetra hydrocannabinol, trigonelline, choline, cannabinol, cannabidiol	Narcotic, sedative, analgesic,
Male Fern (Filix mas, Aspidium)	Rhizomes of Dryopteris filix-mas F:Polypodiaceae	Filicin, filicin acid, aspidinol, filicotannic acid	Anthelmintic, taenihafuge, expulsion of tapeworms
Jalap	Dried tubercles Ipomoea purge F:Convolvulaceae	Jalapin, convolvulin, tiglic acid,	Cathartic,
Ipomoea	Roots of Ipomoea orizabensis F:Convolvulaceae	Jalapin, ipuranol, ipurganol	Carminative,
Podophyllum	Rhizomes, roots of Podophyllum hexandum F:Berberidaceae	Podophyllin, α,β-peltatins, production o etoposide (semi syn)	Venereal warts, purgative; etoposide in testicular & Lung cance
Kaladana (Pharbitis seeds)	Seeds of Ipomoea hederaceae	pharbiticin,	Cathartic
Colosynth (Bitte apple, bitter cucumber)	Fruit of citrullus colocynthis F:cucurbitaceae	α-Elaterin; colocynthin,	Purgative, carminative
Benzoin (Loban)	Styrax benzoin (Sumatra); S tonkinesis (Siam Benzoin)	Balsamic acids (Benzoic & cinnamic acids); sumaresinolic acid	Expectorant, carminative, diuretic, antiseptic, in respiratory tract infections
Tolu Balsam	Trunk of Myroxylon balsamum F:Leguminosae	Cinnamic acid, cinnamicin, benzyl benzoate; vanillin	Expectoant, flavoring agent, antiseptic; in cough mixtures
Myrrh	Commiphoa molmol	α,β,Ɣ-commiphoric acid,	Stimulant, antiseptic;

	F:Burseraceae	cuminic aldehyde,	in mouthwashes
Storax	Liquidambar orientalis F:Hamamelidaceae	Storesin, cinnamic acid; cinnamyl cinnamate, vanillin,	Stimulant, antiseptic, flavoring agent,
Tar	Bituminous liquid wood of Pinus sylvestris F:Pinaceae	Hydrocarbons, methyl esters,	Expectorant, antipruritic, antibacterial; eczema;
Guggul	Stem bark of Commiphora weightii F:Burseraceae	Steroids, diterpenoids; myrcene, caryophylline; guggulsteone, guggulsteol I, II & III	Anti-inflammatory, anti rheumatic, hypolipidemic,
Boswellia (sallaki guggul)	Boswellia serrata F:Burseraceae	Anisaldehyde, d-α-thujone, β-boswellic acid,	Rheumatoid arthritis; to regain integrity of joints from damage
Colophony (Rosin, gum rosin)	Pinus species F:Pinaceae	Sapinic acid, pimaric acid, Abietic acid	Stimulant, diuretic,
Balsam of Peu (Peruvian Balsam	Myroxylan balsamum F:Leguminosae	Cinnamein, traces of styrene, vanillin, coumarin; cinnamic acid	In scabies, wounds, ulcers, bedsores,
Lac (Shellac)	Resinous secretion of Lacifer lacca	Shellolic acid, aleuritic acid; kerrolic & butolic acid	Used in mfr of sustained release products

CHEMICAL TESTS:

Camphor: Vanillin solution + H2SO4 + campho -> Yellow color change to Blue (synthetic camphor does not give this test)

Chenopodium Oil: Heat 1ml Chenopodium oil in test tube with a piece of porcelain. Deep Golden yellow liquid is produced.

Cinnamon: volatile oil + FeCl3 → Pale green color (Cinnamic aldehyde gives brown color, eugenol gives blue color).

- Cassia oil contains only cinnamic aldehyde, gives brown color.

Jatamansi: 80% alcoholic extract of drug **UV LIGHT->** Bluish-white fluorescence

RASNA: 1 gm rasna + 60% alcohol → filter **UV LIGHT→** Bright bluish white fluourescence.

Gaultheria Oil:

- Oil + vanillin in alcohol + alcohol → Blood Red color

CLOVE: TS Clove + KOH → needle shaped crystals of potassium eugenate observed.

CUBEB: Cubeb + H2SO4 → Purple color produced.

SAFFRON:

- Stigma + H2SO4 → blue color change to purplish-red.
- Saffron + Water → yellowish orange color

TURMERIC:

- Powdered drug + H2SO4 → crimson color
- Turmeric aqueous solu + Boric acid → reddish brown color
- Turmeric + acetic anhydride + H2SO4 → Violet color, when test is observed under **UV LIGHT** → Red fluorescence

ASAFOETIDA:

- Drug + H2SO4 → red/reddish brown color
- Drug + H3NO3 → green color

BENZOIN:

- Alcoholic solution of benzoin with water gives Milky white solution
- Heat Benzoin in test tube with glass plate covering, cool the test tube, and examine under microscope, crystals of cinnamic acid observed.

Tolu Balsam:

- When heated & pressed in between glass slides & examined under microscope, it exhibits crystals of cinnamic acid.
- Alcoholic solution of balsam of Tolu + add $FeCl_3$ → Green color

STORAX:

- Storax + sand + $KMnO_4$→ Benzaldehyde odour
- Storax + Potassium chromate + H_2SO_4 → Odour of Benzaldehyde

TAR:

- Aqueous solution is acidic to litmus.
- Tar + water + heat → Filterate + $FeCl_3$ solution → Red Color produced

ADULTERANTS/Substitutes:

Chenopodium Oil	Substitute: Ch. Album
Turpentine Oil	Resin oil, wood turpentine, petroleum jelly
Caraway (fruit in mericarp form)	Substitute: Indian Dill fruits (cremocarp) & Cuminum cyminum fruit (contain cuminic aldehyde)
Cardamom	Adulterants: Elettaria cardamom var major (Longwild native cardamom; korarima cardamom (seeds do not show rugae)
Dill	Substituted by Indian Dill (Anethum sowa), a cremocarp
Nutmeg	M malabarica, M argentea, M beddomei; M attenuate
Cinnamon Bark	*Jungle Cinnamon*: *Cinnamon chips*: heavy cork cells *Saigon cinnamon*: bark is grayish brown color with light patches & sweet taste. Java Cinnamon: Medullary rays contain tubular crystals of calcium oxalate
Rasna	*Alpinia galangal:* less pungent, does not contain flavonoids
Musk	*Beaver, civet, American musk* ***Herbal plant Musk mallow (Abelmoschus moschatus)***
Sandal wood oil	*West Indian Sandalwood; Australian sandal wood oil*
Clove	***Adulterants****:*

	Mother cloves: Dark brown fruits, contains starch *Blown cloves*: expanded flowers of clove tree; Exhausted cloves:
Saussurea	*Vetiver oil*
Crocus	***Adulterants****:* Florets of safflower (Carthamus tinctoria)
Male Fern	Rhizomes of Athyium filix-foemina (Dumb bell shaped vascular bundles)
Ipomoea	Adulterated by Ipomoea tuberosa (under UV light shows deep bluish violet color)
Guggul	Commiphora species like C abyssinica, C roxburgii

ALKALOIDS

Alkaloids are organic products o natural or synthetic origin which are basic in nature and contain one or more nitrogen atoms.

Common Chemical Test for Alkaloids:

Mayer's Reagent ($KHgI_2$solution): Cream color precipitate
Dragendorff's Reagent ($KBiI_2$ solution): Reddish Brown color precipitate
Wagner's Reagent (I-KI solution): Reddish brown color precipitate
Hager's Reagent (Picric acid): Yellow colored precipitates.

Drug Name	Biological Source	Active Constituent	Uses
INDOLE ALKALOIDS			
Ergot	Fungal sclerotium of Claviceps purpura in rye plant Secale Cereale	Ergometrine, Ergotamine	Oxytocic, prevents post partum hemorrhage; used in migraine
Nux Vomica (Crow fig)	Dried ripe seeds of Strychnos nuxvomica F:Loganiaceae	Strychnine, Brucine; vomicine, strychnicine α-colubrine	Bitter stomachic, tonic; CNS, respiratory,cardiac stimulant; increase BP in cardiac failure;
Physostigma (Calabar bean)	Ripe seeds of Physostigma venenosum F:Leguminosae	Eserine; Eseramine, physostigmine, eseroline;	Parasympathomimetic, Antidote for tricyclic antidepressants
Rauwolfia (Chhotachand,	Dried roots of Rauwolfia serpentine F:Apocynaceae	Reserpine, ajmaline, ajmalicine,	Antihypertensive; in mild anxiety;

Sarpagandha)		yohimbine, serpentine	ajmalicine used in circulatory diseases
VINCA (Periwinkle)	Whole plant of Catharanthu8s roseus F:Apocynaceae	Vincristine, Vinblastine; catharanthine	Antineoplastic agent, in treatment of acute leukemia, hodgkin's diseases, reticulum cell sarcoma,
ISOQUINOLINE ALKALOIDS			
Opium	Unripe capsules of Papaver somniferum F:Papaveracea	Narcotine, Narceine, Papaverine; Morphine, Codeine, Thebaine	Hypnotic, sedative, analgesic; codein is antitussive; Apomorphine emetic
Curare (South American arrow root)	Chondrodendron tomentosum; Strychnos castelnea, F:Loganiaceae	Tubocurarine, curine, curarine, cycleaning	Skeletal muscle relaxant; used in surgical operations; diagnosis of myasthenia gravis
Ipecacuanha (Ipecac)	Rhizomes & roots of Cephaelis ipecacuanha F:Rubiaceae	Emetine, cephaeline, emetamine,	Expectorant, emetic;
TROPANE AKLALOIDS			
Belladonna (Deadly night shade leaf	Dried leaves of Atropa belladonna ***F:Solanaceae*** (Antidote for chloral hydrate & opium poison)	l-hyoscyamine& Atropine, belladonine,	Parasympatholytic; reduce secreations of sweat,saliva, gastric jujice, reduce spasms in intestinal gripping
Datura	Leaves & flowering tops of Datura metel F:Solanaceae	Hyoscine (Scopolamine), l-hyosciamine	Parasympatholytic; CNS Depressant effect; in cerebral excitement
Hyoscyamus (Henbane)	Leaves & flowering tops of Hyoscyamus niger F:Solanaceae	Hyoscyamine; atropine, hyoscine,	As Counteract gripping; relieve urinary spasms, expectorant
Stramonium (Thorn apple leaf)	Leaves & flowering tops of Datura Stramonium	l-hyoscyamine & hyyoscine; atropine	In Asthma; control salivation, muscular rigidity, tremors in parkinsonism
Duboisia	Leaves of D myoporoides F:Solanaceae	Scopolamine, Atropine;	-
Coca Leaves	Erythroxylon coca, F:Erythroxylaceae	Cocaine, cinnamoyl cocaine, α truxilline; Ecgonine	Cocaine local anesthetic, reduce sedative, respiratory depressant effects of morphine,

QUINOLINE ALKALOIDS			
Cinchona (Jesuit/ Peruvian Bark)	Cinchona calisaya F:Rubiaceae	Quinine, quinidine, cinchonine, cinchonidine	Antimalarial, antipyretic, bitter stomachic; Quinidine a cardiac depressant, in arrhythmias, tachycardia & in AF
Camptotheca	Stem wood of Camptotheca acuminate F:Nyssaceae	Camptothecin	DNA topoisomerase I inhibitor; in cancer
AMINO ALKALOIDS			
Ephedra (Ma-Huang)	Stems of Ephedra gerardiana F:Gnetaceae	Ephedrine, Nor-ephedrine,	Bronchodilator, in asthma, in allergic conditions;
Colchicum (Meadow saffron seeds)	Ripe seeds of Colchicum luteum, c autumnale F:Liliaceae	Colchicine, demecolcine	In gout & rheumatism; antitumor;
Gloriosa (Glory Lily)	Tubers of Gloriosa superba F:Liliaceae	Colchicine	Gout & inflammation
PYRIDINE ALKALOIDS			
Lobelia (Indian tobacco, asthma weed)	Lobelia nicotinaefolia F:Campanulaceae	Lobeline, Loelidine, Lobelanine,	Asthma, respiratory stimulant,
Areca nut (betel nut)	Ripe seeds of Areca catechu F:Palmae	Arecoline, Arecaidine, guvacoline,	Parasympathomimetic, sialogogue; anthelmintic, vermicide, taenifuge
PURINE ALKALOIDS			
Coffee (Coffee bean)	Ripe seed of Coffea Arabica F:Rubiaceae	Caffeine,	Stimulant, diuretic
Cocoa	Seeds of Theobroma cocoa F:Sterculiaceae	Theobromine, caffeine,	Stimulant, diuretic, nutritive
Kola (Bissy or Gooroo seeds)	Cola nitida F:Sterculiaceae	Caffeine, theobromine, kolacatechin	In beverages, stimulant
Tea	Leaves & leaf buds of Thea sinensis F:Theaceae	Caffeine, gallotannic acid, theobromine	CNS Stimulant, cerebral vasoconstrictor
IMIDAZOLE ALKALOIDS			
Pilocarpus (Jaborandi)	Leaves of Pilocarpus spe F:Rutaceae	Pilocarpine, isopilocarpine, pilosine, isopilosine	Antagonist of atropine; in treatment of glaucoma,
Veratrum	Veratrum viride	Cereveratrum,	Lowers BP, decrease

	(American), V album (white/European hellebore F:Liliaceae	cevadine, germerine, protoveratrine A & B	Heart Rate,
Kurchi (Holarrhena)	Bark of Holarrhena antidysenterica F:Apocynaceae	Conessine (kurchicine), norconessine, isoconessine, holarhimine,	Antiprotozoal, in treatment of amoebic dysentery.
Ashwagandha (Withania, Asgandh)	Roots & stem of Withania somnifera F:Solanaceae	Withanine, somniferine, somnine; steroidal withanolides withaferin, Withaerin A& D	Sedative, hypnotic; hypotensive, immune modulatory agent; sitoindoside show anti stress; nervine & skin diseases
Aconite (Bachnag, Monkshood)	Dried root of Aconitum napellus F:Ranunculaceae	Aconitine, neopelline, napelline,	Neuralgia, sciatica, rheumatism, inflammation
QUINAZOLINE DERIVATIVES			
Vasaka (Adhatoda, Adulsa, Malabar nut)	Leaves of Adhatoda Vasica F:Acanthaceae	Vasicine, vasicinone,	Expectorant, bronchodilator, irritant, vomiting, diarrhea; oxytocic, abortifacient
Punarnava (Rakta punarnava, Hog weed)	Boerhaavia difussa F:Myrtaceae	Punarnavine, punernavoside, antifibrinolytic agent	Diuretic, expectorant, in jaundice
Shankhpushpi (Shankhvel)	Canscora decussata F:Gentianaceae	Bitter substance, oleo-resin,	Nervine tonic, epilepsy, nervouis debility

DISPENSING PHARMACY

Temperature:

Cold temperature: 2°c to 8°c

Cool temperature: 8°c to 25°c

Room temperature: temperature prevailing in working area

Warm temperature: 30°c to 40°c

Pharmaceutical Calculations:

1 Nanogram = 10^{-9}gm

1 microgram = 10^{-6}gm

1 milligram = 1/1000 gm

I. Avoirdupois system:

• 1 Ounce (Oz) = 437.5 grains • 1 pound (lb) = 16 ounces • 1 stone = 14 pounds	1 fluid dracham = 60 minims 1 fluid ounce = 8 fluid drachm 1 pint = 20 fluid ounces 1 quart = 2 pint 1 gallon = 4 quarts

II. Apothecaries Measurement:

- 1 scruple = 20 grains
- 1 drachm = 3 scruples
- 1 ounce = 8 drachms
- 1 pound = 12 ounces

Household Measurement:

- 1 drop = 1 minim = 0.04 ml
- 1 teaspoonful = 1 fl. dr = 5 ml
- 1 desertfulspoonful = 2 fl.dr = 8 ml

- 1 Tablespoonful = 4 fl. dr = 15 ml
- 1 wineglassful = 2 fl. Oz = 60 ml

Proof Spirit: An aqueous solution containing 57.1% v/v of absolute alcohol is called proof spirit.

ISOTONIC SOLUTION: Two solutions having same osmotic pressure are called Iso-osmotic/Isotonic solutions. Ex. 1.8% solution of urea, 0.9% NaCl solution are same osmotic pressure as that of body fluids.

POSOLOGY

For calculation of dose of children:

Young Formula = $\frac{Age\ in\ Years}{Age+12}\ x\ Adult\ dose$

Dilling Formula = $\frac{Age\ in\ years}{20}\ x\ Adult\ dose$

Fried's Formula = $\frac{Age\ in\ months}{150}\ x\ Adult\ dose$

Clark's Formula = $\frac{Weight\ in\ Pounds}{150}\ x\ Adult\ dose$

Based On Surface Area, children dose can be calcuated as:

$$\frac{BOdy\ surace\ area\ of\ child}{1.73}\ x\ Adult\ dose$$

PRESCRIPTIONS

Parts of Prescription:

i. Physician Info
ii. Patient info
iii. Superscription: Symbol Rx (take thou = you take)
iv. Inscription: comprises important part of drug names, quantity, dose, dosage form etc.

v. Subscription: specific directions to Pharmacist on how to compound the medication
vi. Transcription: instruction given to patient
vii. Renewal: No. of times a prescription is to be repeated, is written by physician under renewal instructions.
viii. Signatura: Signature of prescriber.

LATIN TERM	Abbreviation	English Meaning
Aurinarin	Aurin	An ear cone
Auristillae	Auristill	Ear drops
Buginarium	Buginar	Nasal drops
Capsula	Caps	A capsule
Capsula amylacea	Caps. Amylac.	A cachet
Capsula gelatin	Caps. Gelat.	A gelatin capsule
Cataplasma	Cataplasm	A poultice
Cereolus	Cereol	An urethral bougie
Collanarium	Collum	A nose wash
Collutorium	Collut	Mouthwash
Collyrium	Collyr	Eye lotion
Cremor	Crem	A cream
Emulsio	Emul	An emulsion
Gargarisma	Garg.	A Gargle
Guttae	Gtt.	Drops
Haustus	Ht.	Draught
Inhalatio	Inhal.	An inhalation
Injectio	Inj.	An injection
Insufflatio	Insufl	An insufflation
Linctus	Linct.	A liniment
Lotio	Lot.	Lotion
Mistura	M, mist.	Mixture
Nebula	Neb	Spray solution
Oblatum	Oblat	A cachet
Pasta	Past.	A paste
Pastillus	Pastill.	A pastill
Pessus	Pess.	A pessary
Pigmentum	Pigm.	A paint
Pilula	Pil.	A Pill

Pulvis	Pulv	A powder
Conspersus	Consper	A dusting powder
Sternutamentum	Sternut.	A snuff
Suppositorium	Suppos.	A suppository
Tabletta	Tab.	A tablet
Trochisus	Troch.	A lozenge
Ungentum	Ung	An ointment
Nomen proprium	n.p.	Proper Name

Fiat	Ft.	Let it be made
Misce/Miscenture	m.	Mixture
Misce fial mixture	m.fl.m	Mix to make mixture
Fiat pulvis subtilis		Make fine powder
Tere/terature	Ter.	Rubbed
Tere bene simul	Ter. Bene. Sim.	Rubb well together
Capiendus		To be taken
Dandus		To be given
Talis/Tales		Such
Mittae		Send
Deglutindus		To be swallowed
Infricandus		To be rubbed in
Pestillandus		To be droped in
Miscendus		To be mixed
Sugendus		To be sucked
Sumendus		To be taken
Ut antem	u.a.	As before
Utendus	Utend.	To be used
Bis in die	b.i.d/b.d.	Twice a day
Ter in Die/Ter die	T.i.d./t.d.	Thrice a day
Quarter in die	q.i.d./qd	4 times a day
Bis terve in die	b.t.i.d	2-3 times a day
Ter quaterve die	t.q.d	¾ times a day
Quotidie/indies	Quot/indies	Daily

Prima luce/prima mane	Prim. Luc/prim m.	Early in the morning

Mane	M	Morning
Omni mane	o.m.	Every morning
Jentaculum	Jentac.	Breakfast
Omni nocte	o.n	Every night
Hora decubitus	h.d.	At bed time
Nocte manqué	n.m.	Night & morning
Hac nocte	Hac. Noct.	To night
Omni hora/omni singular	o.h./o.s.	Every hour
Omni alterna hora/quaque alterna hora	o.alt.h/qu.alt.h	Every alternative day
Omne quarta hora	o.q.h.	Every fourth hour
Anti cibos	a.c.	Before meals
Ante cibum	a.c.	Before food
Post cios	p.c.	After food
Inter cibos	i.c.	Between meals
Lente		Slowly
More dicto	m.d.	As directed
Pro re nate	p.r.n	Occassionally
Si opis sit	s.o.s	When required
Tussi urgent	Tuss. Urg	When cough is troublesome
Parti affectoe	p.a.	To the affected part
Sinister/laerus	Sinist/laev	Left
Ocularis	Ocul.	For the eyes

SOLID DOSAGE FORM

Powders Classication:

I. Bulk powders for external use: dusting powders, snufs, dental powders, insufflations
II. Bulk powders for internal use
III. Single & compound powders for internal use
IV. Effervescent granules
V. Cachets

Dusting Powders: Used for externally for local applications not intended or systemic action. Dusting powders contains ZnO, starch, Boric acid/natural mineral substances such as kaolin/talc.

Snuffs: These are finely divided solid dosage forms of medicaments dispensed in flat metal boxes with hinged lid.

Douche powders: These are intended to be used as antiseptics or cleaning agents for body cavities.

Dental powders: These contain detergents, abrasives, antiseptics, coloring & flavoring agents.

Insufflations: These meant for applications to the body cavities, now a days these are given in aerosol form.

Bulk powders contain many doses in a wide-mouthes container suitable for remove the powder by teaspoon. Ex: Antacids, Laxatives, Purgatives.

Simple & Compound Powders: These are unit dose powders packed in envelops, metal foil, small heat-sealed plastic bags.

Effervescent granules: These preparations supplied either by compounding the ingredients as granules/dispensed in the form of salt. The ingredients react in presence of water evolving CO_2 gas, $NaCO_3$ and citric/tartaric acid is used in preparation.

Cachets: It is a unit dosage form, made of flour & water so damaged easily. The drug is place in one of two halves of cachet, the upper half is then placed over it & pressed with help of suitable device.

Eutectic Mixtures: Some of drugs which tend to liquefy on mixing called “Eutectic Mixtures”.

PASTILLES: Pastilles are preparations which are kept in the mouth & slowly allowed to dissolve thus gradually releasing the medication for local action generally in the throat. The base is composed of glycerin & gelatin.

LOZENGES: They are sacked in the mouth to disintegrate slowly releasing the medication for local action.

TABLETS

Compounding of Tablets: Tablets contains following ingredients.

a) ***Diluents***: To increase bulk and convert in the compressible form ex: dibasic calciumphosphate, calcium sulphate, lactose spray dried, mannitol, sorbitol, dextrose.
b) ***Binders & Adhesives***: These are used in dry/liquid form to reduce amorphous nature of substance & convert into compressible form (Wet granulation). Ex: Acacia, Tragacanth, Methyl cellulose, HPMC, Starch, Sorbitol
c) ***Disintegrating agents:*** These facilitate disintegration of tablet in gastrointestinal tract. Ex: veegum HV, Methyl cellulose, Isapghul, Alginic acid, sodium dodecyl sulphate, Ion exchange resin.
d) ***Glidants:*** Act as flow promoter & reduce friction between particles Ex: talc, starch, Magnesium stearate, Calcium stearate, Boric acid, NaCl, Lycopodium
e) ***Lubricants:*** These reduce inter-particular friction. It improves ejection of tablet from die wall & reduce sticking problems & smooth tablets are produced. Ex: talc, Mg stearate, PEG
f) ***Antiadhesives:*** These are used to reduce adhesion of tablet surface to dies & punches during compression of tablet.
g) ***Coloring Agent:***
h) ***Flavoring agent*****:** Ex Cinnamon, Coriander, Caraway
i) ***Sweeteners:*** Ex: Sodium saccharoin, Aspartame, Sugar

TABLET DEFECTS:

Capping: Partial/complete separator of top/bottom surface of tablet from main body. This is due to entrapment of air, incorrect set up of tablet press.

Lamination: Separation of tablet into 2-3 layers.

Picking: Removal of surface material from punch surface

Sticking: Some material stick to die wall

Chipping: The tablet produced, has rough surace due to this problem. It creates difficulty in free movement of punches.

Mottling: Unequal distribution of color in tablet is called mottling.

Poor flow: Incomplete filling of dies by powder material due to poor flow of material from hopper to die wall.

Double Impression: One dark & one lighter impression on tablet surface are called double impression.

Phases of Sugar Coating:

Sealing: The basic object is prevent the core tablet from water during subsequent steps in sugar coating. By depositing shellac/cellulose acetate phthalate (CAP).

Sub-coating: By wetting the tablet with adhesive solution, dusting with filler & drying to remove moisture. The purpose is to round the tablet contour & provide bond between seal coat & sugar coat. Ex: Aqueous solution of sugar, corn syrup & Acacia.

Syrup Coating:

Polishing: Polishing is carried out in canvas lined coating pans & the process consists of applying thin layer of waxy materials to impart shine to the finished tablets. Ex: Bees wax, Carnauba wax, synthetic chlorinated wax.

Film Coating: Polyvinyl pyrrolidine, carboxy acetate derivatives, methacrylates, CMC, HPMC & Ethyl cellulose.

Film Defects:

Blistering: Unsmooth film surface shows a number of uneven spots called blisters.

Bridging: This may occurs with monogrammed/bisected tablet due to lack of adhesion of film to tablet surface.

Orange Peel: Appearance of surface resembling the peel of orange due to improper distribution of coating solution.

Flaking: Easy removal of coating material from product in sheet/large flakes.

Bloom: Development of a dull film/bloom is called blooming. It is due to processing of product under humid conditions.

Spotting: It occurs due to migration of plasticizers, dyes or other additives in the coating formulae, to the coat.

CAPSULES

Capsule shells are made of gelatin, the consistency of which may be adjusted by addition of substances like glycerol, sorbitol and other exicipients.

Two types of gelatin capsuels are there:

1.Hard Gelatin Capsules: It consits 2 pieces, a cap and a body. Empty caps are sold by sizes from 000 (the largest) to the size 5 (smallest).

Caps shells are prepared by 2 methods: a)plate process b)rotary dice process

Rotoweigh: Capsule weighing machine

Rotosort: Filled caps cleaning & polishing machine

Harnett Model B & Markem Model280 A are capsule imprinting machines.

2. Soft Gelatin Capsules: The shells of soft capsules are thicker than hard capsules. It constitutes single part and various shapes.

LIQUID DOSAGE FORM

Classification:

I. Internal Liquid preparations
   a)Monophasic: Ex: syrups, elixirs, solutions, linctuses
   b)Biphasic: suspensions, emulsions

II. External Liquid Preparations:

a) Applied on skin: Lotions, liniments, throat paints, collodions
b) Instilled into body cavities: Enema, douches, ear, nasal drops, inhalation
c) Used in mouth: Gargles, Mouth washes.

Syrups: These are concentrated oral solution of sugar/sucrose in water or other aqueous liquids.

Elixirs: Elixirs are clear, liquid, flavored hydroalcoholic preparations intended for oral use. Two types.

a)**Non medicated**: These are used purely as diluting agents/solvents for drugs containing 25% alcohol Ex: simple elixir, Isoalcoholic elixir.

b) **Medicated elixir**: Elixir contain therapeutically active ingredients. These elixirs used as mostly cough syrup prepartions.

Formulation of Elixir:

i)Vehicle: 10-20% alchol

ii)Stabilizers: Disodium edetate, citric acid etc.

iii)coloring agents: Amaranth for magnetic red, compound tartrazine for saffron, tartrazine for green color etc.

iv)Flavoring agent: Conc respberry juice, black current syrup

v)Preservatives: Benzoic acid, parahydroxy benzoic acid.

SOLUTIONS:

A solution is a homogeneous one phase system consist one or more components. It contains two phase ie. Solvent and solute.

Formulation:

i)Solvent: a)aqueous

b)Non aqueous: Fixed oil, polyhydric alcohol, ethyl ether, liquid paraffin

ii)Buffers: carbonates, citrates, gluconate, lactates, phosphates, tartrate etc.

iii)Colors: Water soluble dye amaranth

iv)Density modifiers

v)Flavors & Perfumes

vi)Taste:

a)salty: Apricot, butterscotch, liquorice, peach, vanilla

b)Bitter: Anice, Chocolate, mint, wild cherry

c)Sweet: vanilla fruits

d)Sour: citrus, raspberry

vii)Preservatives

viii)antioxidants & reducing agents.

LINCTUSES:

Linctuses are solutions of one or more medicament, usually containing large amount of sucrose & also have a demulcent effect on mucous membranes of throat. They should be administered undiluted and sipped and swallowed slowly.

Formulation:

a)vehicle: syrup, glycerine, throat syrup, chloroform water, sorbitol

b)stabilizer: syrups

c)Coloring agent: coal tar dyes, compound tartrazine solutions

d)Flavoring agent: lemon syrup, tolu syrup etc.

e)Preservatives: Benzoic acid, chloroform spirit, cinnamic acid, tolu syrup etc.

LOTIONS:

Lotions are usually liquids or liquid suspensions or semi solid preparations containing one or more medicaments intended to be applied to uniform skin without rubbing.

Formulation:

Bentonite – suspending agent.

Methyl cellulose/sod carboxy methyl cellulose - used to hold active ingredient in contact with affected area.

Glycerin: Keep the skin moist for considerable period of time

Alcohol: Used for accentuated action like drying, cooling etc.

Miscellaneous: Benzocaine, calamine, sulphur, Zinc oxide etc.

Labelling: Shake well before use, For external use only

LINIMENTS:

Liniments are solutions or mixtures of various substances in oil, alcohol solutions of soap or emulsions or occasionally semi-solid preparations for external applications should be labeled. They are applied with rubbing/massaged into the skin as counter irritants/stimulating agent to the affected are & because of this were known as embrocations.

Two types of vehicles are used i)alcohol : soap liniment, aconite liniment

ii)Oils: ex camphor liniment, methyl salicylate liniment.

Labeling: “Shake well before use”, “For external Use” “Not to be applied to wounds or before skin”.

THROAT PAINTS:

Paints are solutions or dispersions of one or more medicaments intended for application to skin/in some cases to mucous membrane. They contain volatile solvent that evaporates quickly to leave dry or resinous film of medicament. Ex: Mandl’s paint, Tannic acid glycerin paint, coal tar paint, compound mastric paint.

Labeling: For External Use only.

COLLODIONS:

Liquid preparations for external use, containing pyroxylin in a mixture of ethyl ether and ethanol. They are applied to skin by a soft brush or suitable applicator.

a)Medicated: Salicylic acid collodions, used as keratolytic agent used in treatment of corns & warts.

b)Non medicated: For protection of small cuts & scratches.

Flexibility of collodion is made by addition of castor oil & camphor. It has been used to reduce/eliminate side effects of fluorouracil treatment of solar keratoses.

Label: “highly inflammable, keep away from naked flames” “For external use only”.

DOUCHES:

A douche is an aqueous solution directed against a part or into a cavity of body. If powder or tablet are employed for this purpose, they must e completely solution in water.

Douches are mainly used as:

a)antiseptic: Chlorhexidine, Lactic acid, Mercuric chloride, chloroxylenol

b)Astringent: Alum, Tannic acid, Zinc sulphate

c)Cleaning: NaCl, Boric acid, saponated cresol

d)soothing agent.

ENEMAS:

Enemas are aqueous or oily solution or suspension that are employed to evacuate the bowel, to influence the general system by absorption or to affect locally the seat of disease introduced into the rectum for cleansing therapeutic or diagnostic purpose.

GARGLES:

Gargles are aqueous solutions used for treating the pharynx and nasopharynx by forcing air from lungs through the gargle that is held in throat, they are generally dispensed in concentrated form. They must be diluted with water prior to use.

MOUTHWASHES:

An aqueous solution which is often used for its deodorant refreshing or antiseptic effect. It contain antibacterial substances.

a)Antibacterial agent: Alkaaline phenol, Hydrogen Peroxide, Buffered sodium perborate, thymol glycerine.

b)Astringents: Zinc sulphate, Zinc chloride etc.

SUSPENSIONS

A biphasic liquid dosage form in which finely divided solid particles are suspended in a liquid medium. Dispersed solid particles are known as internal phase & dispersions medium is known as continuous or external phase. 2 types of Suspensions:

Flocculated Suspensions	Deflocculated Suspension
• Particles form loose aggregates & settle down in container • Rate of sedimentation is high, since particles settle as a floc, which is a collection of particles • A sediment is formed rapidly within minutes • Sediment loosely packed and possess scaffold like structure. Particles do not bind tightly to each other & a hard dense cake does not form. • The suspension is unslightly due to rapid admin & presence of obvious, clear supernatant region.	• Particles exist in suspension from as separate entities • Rate of sedimentation is slow, fine each particles settle separately & particle size is minimal • A sediment is formed slowly may take months • Sediment eventually becomes very closely packed, due to weight of upper layers of sedmenting materials. • Suspension has a pleasing appearance because the suspended particles remain suspended uniformly for long time.

Suspending Agent:

i)Organic:

a)Natural: Gum tragacanth, gum acacia, sodium alginate, agar, gelatin, starch

b)Semisynthetic: methyl cellulose, Sodium Carboxy methyl cellulose

ii)Inorganic: Bentonite

iii)Synthetic: Carboxy vinyl polymer.

EMULSIONS

Emulsions are biphasic system consists of 2 immiscible liquids on of which is finely subdivided & uniformly dispersed as droplets throughout the other phase is known as dispersion medium. Dispersion phase also called internal phase, dispersion medium is called external phase.

Types of Emulsions: oil in water, water in oil, Miscellaneous.

Oil in water emulsions: Oil is dispersed phase, aqueous is dispersion medium

Water in Oil emulsions: Water is dispersed phase, oil is dispersion medium.

Oil in Water emulsion	Water in Oil emulsion
Non greasy & easily removable from skin surface	More greasy & not washable with water
They meant for internal use as bitter taste of oils can be masked	They meant for external use like cold cream
Externally applied emulsion provide cooling effect ex; vanishing cream	Externally applied emulsion prevent evaporation of moisture from surface of skin
Water soluble drugs are more quickly released	Oil solutions drugs are more quickly released
Show a positive conductivity test	Do not give positive conductivity test

Emulsifying Agent:

I)Hydrocolloids:

a) Natural Products

Tree exudates: Acacia gum, gum ghatti, karaya gum, tragacanth

Sea weeds: Agar, carrageenan, alginate

Seed extract: Locust bean, guar gum

Steroid containing substances: wool fat, wool alcohol

Animal substances: Gelatin, casein etc

Mineral substances: Bentonite, veegum

b)Inorganic: Colloidal alumina, milk of magnesia, MgO, Mg trisilicate

c)Semi synthetic: Methyl cellulose, carboxy methyl cellulose, HMC, MCC

d)Synthetic: carbopol, colloidal silicone dioxide.

II) **Surfactants**:

A)Anionic:

Carboxylic acid: Soap, acetylates, polypeptide condensates

Sulphuric acid esters: sulfated monoglycerides, alkyl suphates

Alkyl & alkyl-aryl sulfonates: dodecyl benzene sulphonates

Phosphoric acid esters: Triacyl phosphate

Substituted alkyl amide: sarcosinate, taurates

Hemiesters: Sulfosuccinates.

B) Cationic:

Amines: alkoxy alkylamines

Quarternaries: Benzylalkalonium chloride

c)Nonionic:

Polyalkoxy ethers: Polyoxy ethylene alkyl ether, block polymer, soritan esters,glyceryl esters, lauryl alcohol.

HLB Method: For selection of emulsifying agent HLB method (Hydrophilic-Lipophilic Balance) is used. It has 0-18 scale range.

HLB Range	Application
0-3	Antifoaming
4-6	Water in oil emulsifying agent
7-9	Wetting agent
8-13	Oil in water emulsifying agent
13-15	Detergents
10-18	Solubilizing agent

Test for identification of emulsion type:

- Dilution test
- Conductivity test
- Dye solubility test
- Cobalt chloride test
- Fluorescence test

Instability of Emulsion:

a)Cracking/Coalescence: Coalesce is a growth process during which the emulsified particles join to form larger particles. When small particles merged & form large droplets, the emulsion will separate completely & cannot dispersed on reshaking. It is called cracking.

b)Creaming: Under influence of gravity suspended particles/globules tend to upward movement, known as creaming.

SEMISOLID PREPARATIONS

OINTMENTS: These are used for application to skin & usually contain a medicament.

Ointment bases classification:

a)Oleaginous b)Absorption Base c)Emulsion base d)Water soluble base

Oleaginous Bases: These are anhydrous, hydrophobic and are not removable by water.

Hydrocarbons: Petrolatum, liquid paraffin microcrystalline wax

Vegetable Oil & animal Fats: coconut oil, olive oil, peanut oil, sesame oil, almond oil, beeswax, spermaceti wax.

Hydrogenated & sulphated oils: castor, cotton seed, soyabeen, corn oils.

Silicones: dimethyl polysiloxanes, stearyl esters of dimethyl polysiloxane

Alcohols, acids: Cetyl alcohol, oleyl alcohol, lauryl alcohol, myristyl alcohol, stearic acid, palmitic, lauric acid, ethyl oleate, ethylene glycol.

Absorption Base: They can take up large amount of water due to their high water number.

a)Anhydrous : Anhydrous petrolatum, Anhydrous lanolin (wool fat)

b)Hydrous Absorption base : Lanolin, Rose water ointment, cold cream, wool alcohol ointment.

Emulsion Base: Two types water in oil bases, oil in water bases.

Water soluble base: High and low molecular weight poly ethylene glycols known as Carbowax.

CREAMS: It is viscous emulsion of semisolid consistency intended for the application to the skin or mucous membrane. It has opaque appearance while the ointment is translucent. These are washable, and do not form occlusive film.

Two types of creams: Oily cream contains water in oil emulgent which may be wool fat, wool alcohol, fatty acid ester of Sorbitan or Divalent soap. Aqueous cream contain oil in water emulgent which may be emulsifying wax, alkali soap, monostearin or PEG derivative of sorbitan Fatty acid ester.

PASTES: Pastes are ointment like preparation for external application. They contain high insoluble solids, Normal insoluble solids are zinc oxide, starch, calcium carbonate, talc etc. They tend to absorb secretions. Pastes give protective barrier to noxious chemical ammonia.

JELLIES/GELS: Gels are aqueous colloidal suspension of hydrated forms of insoluble medicaments. Jellies are transparent or translucent, non-greasy semi-solid preparation mainly used externally. They contain polymer less than 10%. Polymer can be: Natural like tragacanth, pectin, agar, carrageenan, alginic acid; synthetic like MC, carbopols, CMC, Hygroscopic substances like glycerin, propylene glycol, sorbitol.

SUPPOSITORIES

Suppository is a medicated solid dosage form intended for administration into body cavity except oral cavity. These are used for either local or systemic effects. Their effect is either by local or systemic effects. Their effect is either by melting at body temperature or by dissolving in an aqueous secretions of the mucous membrane and allowing releasing of the active medicament.

Types:

- Rectal suppositories
- Vaginal (Pessaries)
- Urethral (Bougies)
- Nasal bougies
- Ear cone

Types of Suppositories Base:

A) Oleaginous/Fatty
   a)cocoa butter (theobroma oil)
   b)synthetic triglycerides mixture

B) Aqueous base

   a)glycerinated gelatin

b)soap glycerine

c)Macrogol/Carbowax (PEG)

C) Emulsifying Base: Mass esterinum, witespol, massupol.

BIOPHARMACEUTICS

Biopharmaceutics: Study of factors influencing the rate of amount of drug that reaches the systemic circulation and the use of this information to optimize the therapeutic efficacy of the drug products.

Passive diffusion:

- It is also known as nonionic diffusion. It is the major process for absorption of more than 90% of the drugs.
- It is defined as the difference in the drug concentration on either side of the membrane.
- Passive diffusion is best expressed by Fick's first law of diffusion, Which states that the drug molecules diffuse from a region of higher concentration to one of lower concentration until equilibrium is attained and that the rate of diffusion is directly proportional to the concentration gradient across the membrane. It can be mathematically expressed by the following equations:

$$\frac{dQ}{dt} = \frac{\mathrm{DAKm/w}}{h}(\mathrm{CGIT} - \mathrm{C})$$

Where,

dQ/dt = rate of drug diffusion (amount/time). It represents the rate of appearance of drug in blood.

D = diffusion coefficient of the drug through the membrane (area/time).

A = Surface area of the absorbing membrane for drug diffusion

$K_{m/w}$ = Partition coefficient of the drug between the lipoidal membrane and aqueous GI fluids

C_{GIT}-C=difference in the concentration of drug in the GI fluids and the plasma called the concentration gradient (amount/volume)

h = thickness of the membrane(length)

Since under usual conditions of absorption, D, A, $K_{m/w}$ and h are constants, the term $DAK_{m/w}/h$ can be replaced by a combined constant p called as permeability coefficient.

Permeability refers to the ease with which a drug can penetrate or diffuse through a membrane. due to sink conditions, the concentration of drug in plasma C is very small in comparision to C_{GIT}.

$$\frac{dQ}{dt} = PC\mathrm{GIT}$$

Active Transport: Active transport is a more important process than facilitated diffusion in the absorption of nutrients and drugs and differs from it in several respects

- The drug is transported from a region of lower to one of higher concentration i.e, against the concentration gradient or uphill transport.
- Since the process is uphill, energy is required in the work done by the carrier.
- It can be inhibited by metabolic poisons that interfere with energy production like fluorides, cyanide, and dinitrophenol and lack of oxygen etc.
  Ex: Sodium, Potassium, Calcium, iron, glucose, certain amino acids and vitamins like niacin, pyridoxin, and ascorbic acid.

Facilitated Diffusion: It is a carrier mediated transport system that operates down the concentration gradient (downhill transport) but at a much a faster rate than can be accounted by simple passive diffusion. Since no energy expenditure is involved, the process is not inhibited by metabolic process is not inhibited by metabolic poisons that interfere with energy production.

Facilitated diffusion is importance in the absorption of drugs. Examples of such a transport system include entry of glucose into RBCs and intestinal absorption of vitamins B_1 and B_2.

A classic example of passive facilitated diffusion is the GI distribution of vitamin B_{12}.

Ion-pair transport: Another mechanisms that explains the absorption of drugs like quaternary ammonium compounds and sulfonic acids which ionize under all pH conditions, is ion transport.

Despite their low o/w partition coefficient values, such agents penetrate the membrane by forming reversible neutral complexes with endogenous ions of the GIT like mucin.

Pinocytosis(cell drinking):

Orally administered sabin polio vaccine and large protein molecules are thought to be absorbed by pinocytosis. Sometimes an endocyclic vesicle is transferred from one extracellular compartment to another and such a phenomenon is called as transcytosis.

Ex: Cardiac glycosides are absorbed both passively as well as by active transport. The transport mechanism also depends upon the site of drug administration.

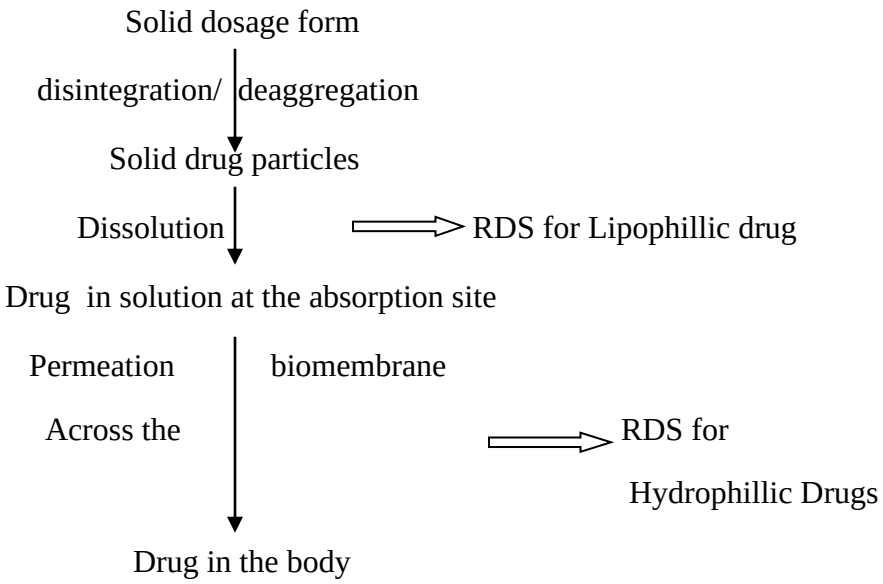
PHYSICOCHEMICAL FACTORS AFFECTING DRUG ABSORPTION:

i.Drug solubility and dissolution rate:

The two critical slower rate-determining processes in the absorption of orally administered drugs are:

1. Rate of dissolution
2. Rate of drug permeation through the biomembrane

Dissolution is the RDS for hydrophobic, poorly aqueous soluble drugs like griseofulvin and spironolactone, absorption of such drugs is often said to be dissolution rate-limited.



Absolute or intrinsic solubility is defined as the maximum amount of solute dissolved in a given solvent under standard conditions of temperature, pressure and pH.

Dissolution rate is defined as thr amount of solid substance that goes into solution per unit time under standard conditions of temperature, pH and solvent composition and constant solid surface area.

Theories of drug dissolution:

Dissolution: is a process in which a solid substances solubilities in a given solvent i.e, mass transfer from the solid surface to the liquid phase.

1. Diffusion layer model/ Film theory
2. Danckwert's model/penetration or surface renewal theory
3. Interfacial barrier model/Double barrier or Limited salvation theory

ii. Particle size and Effective area of the drug:

- Particle size and surface area of a solid drug are inversely related to each other
- Smaller the drug particle, greater the surface area.

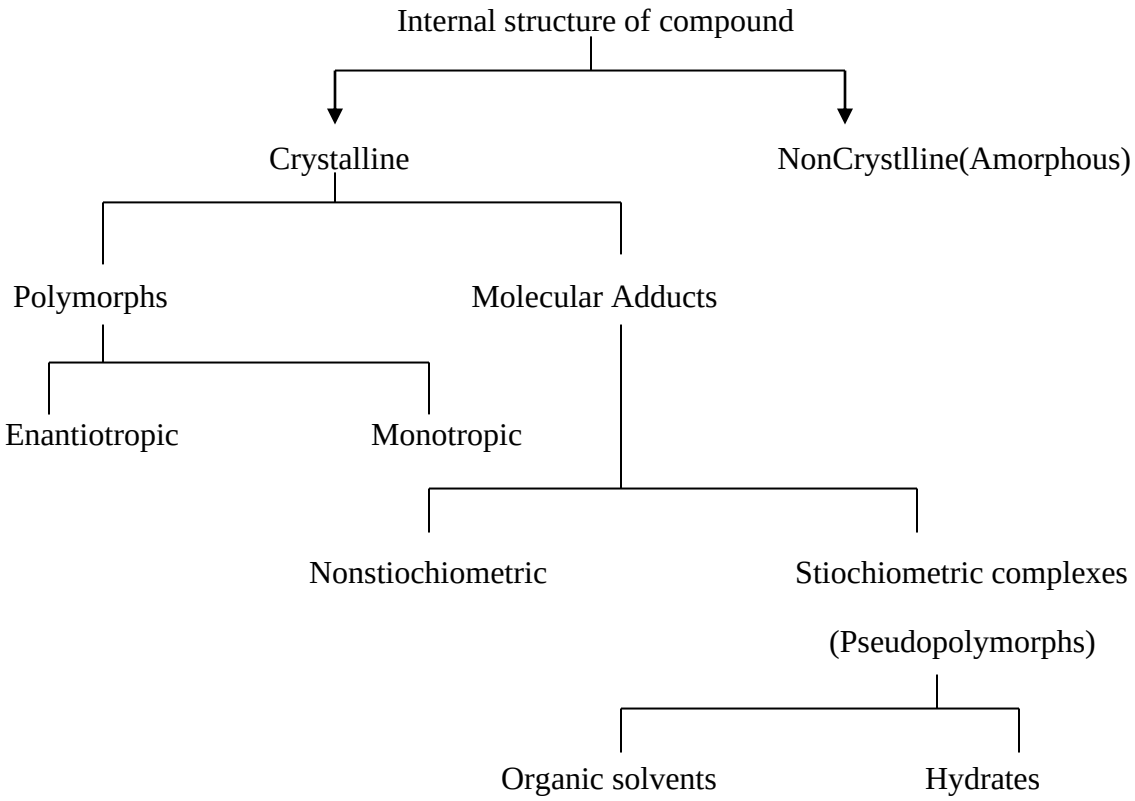
Absolute surface area which is the total area of solid surface of any particle.

Efeective surface area which is the area of solid surface exposed to the dissolution medium.

Particle size reduction and subsequent increase in the surface area and dissolution rate is not always advisable especially when the drug are unstable and degrade in solution form and produce undesirable effects.

iii.Polymorphism and amorphism: When a substance exists in more than one crystalline form, the different forms are designed as polymorphs and the phenomenon as polymorphism.

- **Enantiotropic polymorph** is the one which can be reversibly changed into another form by altering the temperature or pressure e.g: sulfur
- **Monotropic polymorph** is the one which is unstable at all temperature and pressures e.g: glyceryl stearates



Hydrates/Solvents:

- The crystalline form of a drug can be either be a polymorph or a molecular adduct or both.
- The stiochiometric type of adducts where the solvent molecules are incorporated in the crystal lattice of the solid are called as the solvates and the trapped solvent as solvent of crystallization.
- The solvates can exist in different crystalline forms are called as pseudopolymorphs. This phenomenon is called as pseudopolymorphism.
- When the solvent in association with the drug is water, the solvate is known as hydrate.

- The anhydrous form of a drug has greater aqueous solubility than the hydrates and this is because the hydrates are already in interaction with water and therefore have less energy for break-up in comparision to the anhydrates for further interaction with water

Salt form of the drug:

- Most drugs are either weak acids or weak bases.
- It is the earliest approach to enhance the solubility and dissolution rate of such drug is to convert them into their salt forms.
- The principle of in situ salt formation has been utilized to enhance the dissolution and absorption rate of certain drugs like aspirin and penicillin from buffered alkaline tablets.
- The approach is to increase the pH of the microenvironment of the drug by incorporating buffer agents and promote dissolution rate.
- The selection of appropriate salt form for better dissolution rate is also important.

Drug pKa and Lipophilicity and GI pH-pH Partition Hypothesis:

- The process of drug absorption from the GIT and its distribution across all biologic membranes.
- The theory states that for drug compounds of molecular weight greater than 100, which are primarily transported across the biomembrane by passive diffusion, the process of absorption is governed by
  1. The dissociation constant (pKa) of the drug
  2. The lipid solubility of the unionized drug
  3. The pH at the absorption site
- Most drugs are weak electrolytes, their degree of ionization depends upon the pH of the biological fluid.
- If the pH on either side on the membrane is different, then the compartment whose pH favours greater ionization of the drug will contain greater amount of drug, and only the unionized or undissociated fraction of drug, if sufficiently lipid soluble, can permeate the membrane.
- The GIT is a simple lipoidal barrier to the transport of drug.
- Larger the fraction of unionized drug, faster the absorption.
- Greater the lipophilicity ($K_{o/w}$) of the unionized drug, better the absorption.

Drug pK_a and Gastrointestinal pH:

- The amount of drug that exists in unionized form is a function of dissociation constant (pKa) of the drug and pH of the fluid at the absorption site.

For weak acids,

$$\text{pH} = pKa + log\frac{(Ionised\ drug)}{(Unionised\ drug)}$$

For weak bases,

$$\text{pH} = pKa + log\frac{(unionised\ drug)}{ionised\ drug}$$

Drug stability:

- A drug for oral use may destabilize either during its shelf-life or in the GIT.
- Two major stability problems resulting in poor bioavailability of an orally administered drug are degradation of the drug into inactive form, and interaction with one or more different compounds either of the dosage form or those present in the GIT to form a complex that is poorly soluble or is unabsorbable.
- Destabilization of a drug during its shelf-life and in the GIT .

Stereochemical Nature of drug:

- Chiral drugs constitute approximately 60% of the drugs incurrent use.
- It is well established that optical isomers differ in the potency of pharmacological effect.
- Enantiomers possess identical physical and chemical properities despite significant differences in spatial configuration.
- As majority of drugs are absorbed passively, they do not display stereoselectivity.

Drug distribution in the body:

Distribution of drug present in systemic circulation to extravascular tissues involves following steps:

1. Permeation of free or unbound drug present in the blood through the capillary wall and entry into the interstitial/extracellular fluid (ECF).
2. Permeation of drug present in the ECF through the membrane of tissue cells and into the intracellular fluid. This step is rate-limiting and depends upon two major factors:
   a.) Rate of perfusion to the extracellular tissue
   b.) Membrane permeability of the drug.

Protein Binding of Drugs:

The interacting molecules are generally the macromolecules such as proteins, DNA or adipose. The proteins are particularly responsible for such an interaction. The phenomenon of complex formation with proteins is called as **protein binding of drugs**.

Intracellular binding: Where the drug is bound to a cell protein which may be the drug receptor; if so, binding elicits a pharmacological response. These receptors with which drug interact to show response are called primary receptors.

Extracellular binding: Where the drug bind to an extracellular protein but the binding does not usually elicit a pharmacological response. These receptors are called secondary or silent receptors.

Plasma protein-drug Binding:

Albumin > α – Acid Glycoprotein > Lipoproteins > Globulins

Blood proteins to which drug bind:

Protein	Molecular weight	Concentration(g%)	Drugs that bind
HumanSerum Albumin	65,000	3.5-5.0	Large variety of all types of drugs
α_1-Acid Glycoprotein	44,000	0.04-0.1	Basic drugs such as imipramine, lidocaine, quinidine etc
Licoproteins	200,000 to 3,400,000	Variable	Basic, lipophilic drugs like chlorpromazine
α_1-Globulin	59,000	0.003-0.007	Steroids like corticosterone and thyroxine and cyanocobalamine
α_2- Globulin	1,34,000	0.015-0.06	Vitamin A,D,E,and K and cupric ions

Binding of drugs to Human serum Albumin:

The human serum albumin (HSA), having a molecular weight of 65,000 is the most abundant plasma protein (59% of total plasma and 3.5 to 5.0g%) with a large drug binding capacity.

Site1: Also called as warfarin and azapropazone binding site.

e.g: NSAIDs (Phenylbutazone, naproxen, idomethacin), Sulphonamides (sulphadimethoxine, sulphamethizole), Phenytoin, sodium valproate and bilurubin.

Site2: It is also called as the diazepam binding site. Drugs which bind to this region include benzodiazepines, medium chain fatty acids, ibuprofen, ketoprofen, tryptophan, cloxacillin, probenicid etc.

Site3:is also called as digitoxin binding site.

Site4:is also called as tamoxifen binding site.

Binding of drugs to α_1-Acid Glycoprotein:

Also called as the orosomucoid, it has a molecular weight of 44,000 and plasma concentration range of 0.04 to 0.1 g%.

It binds to a number of basic drugs like imipramine, amitriptyline, nontriptyline, lidocaine, propranolol, quinidine, disopyramide.

The molecular weight of lipoproteins varies from 2lakhs to 34 lakhs depending on their chemical composition. They are classified on the basis of their density into 4 categories:

1. Chylomicrons (least dense and largest in size)
2. Very low density lipoproteins
3. Low density lipoproteins
4. High density lipoproteins

Binding to Drugs to Globulins:

Several plasma globulins have been identified as α_1-, α_2-, β_1-, β_2-, γ- globulins.

α_1-globulin: also called as transcortin or CBG (corticosteroid binding globulin), it binds a number of steroidal drugs such as cortisone and prednisone. It also binds to thyroxine and cyanacobalamin.

α_2-globulin: also called as ceruloplasmin, it binds vitamins A,D,E,K and cupric ions.

β_1-globulin: also called as transferring, it binds to ferrous ions.

β_2-globulin: bind to carotinoids.

Binding to drugs to blood cells:

More than 40% of the blood comprises of blood cells of which the major cell component is the RBC.

The RBCs constitute 95% of the total blood cells.

The RBC comprises of 3 components :

1. Heamoglobin: It has a molecular weight of 64,500 (almost equal to that of HAS) but is 7 to 8 times the concentration of albumin in blood. Drugs like phenytoin, pentobarbital and phenothiazines bind to haemoglobin.
2. Carbonic Anhydrase: Drugs known to bind to it are acetazolamide and chlorthalidone.
3. Cell membrane: Imipramine and chlorpromazine are reported to bind with the RBC membrane.

Pharmacokinetics of drug absorption:

Object drugs	Precipitant drugs	Influence on object drugs
1. Complexation and adsorption		
Tetracycline,Flouroquinolones like ciprofloxacin, penicillamine	Antacids, food and mineral supplements containing Al, Mg, Fe, Zn, Bi an Ca ions	Formation of poorly soluble and unabsorbable complex with such heavy metal ions.
Cephalexin, Sulphamethoxaz-ole, trimethoprin, Warfarin and thyroxine	Cholestyramine	Reduced absorption due to adsorption and binding
2. Alteration of GI pH		
Sulphonamides, aspirin	Antacids	Enhanced dissolution and absorp-tion
Ferrous sulphate	Sodiumbicarbonate, calcium carbonate	Decreased dissolution and hence absorption
Ketoconazole, tetracyclines, atenolol	Antacids	Decreased dissolution and bioavailability

3. Alteration of Gut Motility Aspirin, Diazepam, Levodopa, lithium Carbonate, Paracetamol,mexiletine Oral contraceptives	Metoclopramide Antibiotic	Rapid gastric emptying; increased rate of absorption Decreased reabsorption of
4. Malabsorption syndrome Vitamin A, B_{12}, digoxin	Neomycin	Inhibition of absorption due to malabsorption/steatorrhoea caused by neomycin.

Order of process:

The velocity with which a reaction or a process occurs is called as its rate. The manner in which the concentration of drug influences the rate of reaction or process is called as the order of reaction or order of process.

Drug A $\longrightarrow$ Drug B

The rate of forward reaction is expressed as

$$\frac{-dA}{dt}$$

Negative sign indicates that the concentration of drug A decreases with time t. As the reaction proceeds, the concentration of drug B increases and the rate of reaction can also be expressed as:

$$\frac{dB}{dt}$$

If C is he concentration of drug A, the rate of decrease in C of drug A as it is changed to B can be described by a general expression as a function of time t.

$$\frac{dC}{dt} = -KC^n$$

Where, K= rate constant

n= order of reaction

Zero-Order kinetics:

If n=0, equation becomes

$$\frac{dC}{dt} = -K_0 C^0$$

Where K_0= Zero order rate constant (in mg/min)

The zero order process can be defined as the one whose rate is independent of the concentration of drug undergoing reaction i.e. the rate of reaction cannot be increased further by increasing the concentration of reactants.

Rearrangement of equation $dC = -K_0 dt$

Integration of equation gives $C-C_0 = - K_0 t$

$$C = C_0 – K_0 t$$

Where C_O = Concentration at drug at t= 0, and

C = Concentration of drug yet to undergo reaction at time t

Zero-Order Half-Life :

Half – life ($t_{1/2}$) or half – time is defined as the time period required for the concentration of drug to decrease by one – half. When $t = t_{½}$, $C = C_0/2$ and the equation becomes

$$C_0/2 = C_0 - K_0 t_{½}$$

We get $t_{1/2} = C_0/2K_0 = 0.5C_0/K_0$

Equation shows that the $t_{1/2}$ of a zero-order process is not constant but proportional to the initial concentration of drug C_0 and inversely proportional to the zero- order rate constant K_0. Since the zero order $t_{1/2}$ changes with the decline in drug concentration, Zero-order equations do not require logarithmic transformations.

First-Order Kinetics:

If n=1, equation becomes

$$dC/dt = -K C$$

Where K = First order rate constant (in time $^{-1}$or per hour)

First order process is the one whose rate is directly proportional to the concentration of drug undergoing reaction i.e. greater the concentration, faster the reaction. It is because of such

proportionality between rate of reaction and the concentration of drug that a first-order process is said to follow linear kinetics.

Rearrangement of equation yields

$$dC/C = - K\, dt$$

Integration of equation gives

$$In\ C = In\ C_0 - Kt$$

It can also be written in exponential form as

$$C = C_0\, e^{-kt}$$

Where e = natural log base

Since In = 2.303 log, equation can be written as

$$log\ C = logC_0 - Kt/2.303$$

First order Half life:

Substituting the value of $C = C_o/2$ at $t_{1/2}$ in equation and it yields :

$$t_{1/2} = 0.693/K$$

This equation shows that, in constrast to zero order process, the half-life of a first order process is a constant and independent of initial drug concentration i.e. irresepective of what the initial drug concentration is the time required for the concentration to decrease by one-half remains the same. The $t_{1/2}$ of a first-order process is an important pharmacokinetic parameter.

Most pharmacokinetic processes i.e, absorption, distribution, and elimination follows first order kinetics.

Volume of distribution:

A drug in circulation distributes to various organs and tissues. When the distribution process is complete (at distribution equilibrium) different organs and tissues contain varying concentration of drug which can be determined by the volume of tissues in which the drug is present. Since different tissues have different concentrations of drug, the volume of distribution cannot have a true physiological meaning. However there exists a constant relationship between the concentration of drug in plasma, C, and the amount of drug in the body, X.

$$X\ \alpha\ C$$

Or, $X = V_d C$

Where V_d = proportionality constant having the unit of volume and popularly called as apparent volume of distribution. It is defined as the hypothetical volume of body fluid into which a drug is dissolved or distributed. It is called as apparent volume because all parts of the body equilibrated with the drug do not have equal concentration.

Apparent Volume of distribution = Amount of drug in the body/Plasma drug concentration

Or, $V_d = X/C$

Methods for studying drug distribution pattern:

Studies for determining drug distribution pattern includes microdialysis, mass spectroscopy and imaging methods such as whole body autoradiography and positron emission tomography (PET).

Pharmacokinetic Parameters: The three important pharmacokinetic parameters that describe the plasma level-time curve and useful in assessing the bioavailability of a drug from its formulation are

1. **Peak plasma concentration (C_{max}):** The point of maximum concentration of drug in plasma is called as the Peak and the concentration of drug at peak is known as peak plasma concentration. It is also called as peak height concentration and maximum drug concentration .C_{max} is expressed in mcg/ml. The peak plasma level depends upon
    - Dose administered
    - Rate of absorption, and
    - Rate of elimination.
2. **Time of peak concentration(t_{max}):** The time for drug to reach peak concentration in plasma is called as the time of peak concentration. It is expressed in hours and is useful in estimating the rate of absorption. Onset time and onset of action are dependent upon t_{max}. This parameter is of particular importance in assessing the efficacy of drugs used to treat acute conditions like pain and insomnia which can be treated by a single dose.
3. **Area Under the Curve (AUC) :** It represents the total integrated area under the plasma level-time profile and expresses the total amount of drug that comes into the systemic circulation after its administration. AUC is expressed in mcg/ml X hours. It is the most important parameter in evaluating the bioavailability of a drug from its dosage form as it represents the extent of absorption. AUC is also important for drugs that are administered repetitively for the treatment of chronic conditions like asthma or epilepsy.

Clearance: Clearance is defined as the hypothetical volume of body fluids containing drug from which the drug is removed or cleared completely in a specific period of time. It is expressed in ml/min and is a constant for any given plasma drug concentration.

Clearance (Cl) = Elimination rate/Plasma drug concentration

Concept of Clearance: The clearance concept was first introduced to describe renal excretion of endogenous compounds in order to measure the kidney function.

The term is now applied to all organs involved in drug elimination such as liver, lungs, the biliary system , etc. and referred to as hepatic clearance, pulmonary clearance, biliary clearance

The sum of individual clearances by all eliminating organs is called as total body clearance or total systemic clearance.

Renal clearance(Cl_R): It can be defined as the volume of blood or plasma which is completely cleared of the unchanged drug by the kidney per unit time.

Cl_R = Rate of urinary excretion/ Plasma drug concentration

Renal clearance is the ratio of sum of rate of glomerular filtration and active secretion minus rate of reabsorption to plasma drug concentration C.

C = Rate of filtration + Rate of secretion – Rate of reabsorption/ C

Relationship between Renal clearance values and mechanism of Clearance:

Renal Clearance(ml/min)	Renal Clearance ratio	Mechanism of Renal clearance	Example(s)
0 (least value)	0	Drug filtered and reabsorbed completely	Glucose
< 130	Above 0, Below 1	Drug filtered and reabsorbed partially	Lipophillic drugs
130(GFR)	1	Drug is filtered only	Creatinine, inulin
> 130	> 1	Drug filtered as well as secreted actively	Polar, ionic drugs
650	5	Clearance equal to renal plasma flow rate	Iodopyracet, PAH

The total body clearance Cl_T, also called as total systemic clearance, is an additive property of individual organ clearances. Hence,

Total systemic clearance

$$Cl_T = Cl_R + Cl_H + Cl_{Others}$$

Because of the additivity of clearance, the relative contributin by any organ in eliminating a drug can be easily calculated. Clearance by all organs other than kidneys is sometimes known as nonrenal clearance Cl_{NR}. It is the difference between the total clearance and renal clearance.

According to Clearance equation

$$Cl_T = \frac{dX/dt}{C}$$

Substituting $dX/dt = K_E X$ from the equation , we get

$$Cl_T = K_E X/C$$

Since $X/C = V_d$ from the volume of distribution, the equation can be written as

$$Cl_T = K_E V_d$$

Parallel equations can be written for renal and hepatic clearances as

$$Cl_R = K_e V_d$$

$$Cl_H = K_m V_d$$

Since $K_E = 0.693/t_{1/2}$, Clearance can be related to half-life by the following equations

$$Cl_T = \frac{0.693Vd}{t1/2}$$

The noncompartmental method of computing total clearance for a drug that follows one-compartment kinetics is:

For drugs given as i.v. bolus

$$Cl_T = X_0/AUC$$

For drugs given e.v.

$$Cl_T = F\ X_0/AUC$$

For a drug given by i.v. bolus, the renal clearance Cl_R may be estimated by determining the total amount of unchanged drug excreted in urine, X_u^{α} and AUC.

$$Cl_R = X_u^{\alpha}/t_{1/2}$$

Organ Clearance: The best way of understanding clearance is an individual organ level. Such a physiological approach is advantageous in predicting and evaluating the influence of pathology, blood flow, P-D binding, enzyme activity etc or drug elimination. At an orgn level, the rate of elimination can be written as :

Rate of elimination by an organ= Rate of presentation of the organ - rate of exit from the organ

Hepatic Clearance: For certain drugs, the nonrenal clearance can be assumed as equal to hepatic clearance Cl_H. It is gives as :

$$Cl_H = Cl_T - Cl_R$$

It can be written for hepatic clearance:

$$Cl_H = Q_H\, ER_H$$

Where, Q_H= hepatic blood flow

ER_H= hepatic extraction ratio

Bioavailability: The term bioavailability is defined as the rate and extent of absorption of unchanged drug from its dosage form.

If the size of the dose to be administered is the same, then bioavailability of a drug from its dosage form depends upon 3 major factors:

1. Pharmaceutical factors related to physicochemical properities of the drug and characteristics of the dosage form
2. Patient related form
3. Route of administration

C_{max}:

The peak plasma concentration that gives an indication whether the drug is sufficiently absorbed systematically to provide a therapeutic response. It is a function of both the rate and extent of absorption. C_{max} will increase with an increase in the dose , a well as with an increase in the absorption rate.

t_{max} :

The peak time that gives an indication of the rate of absorption. It decreases as the rate of absorption increases.

AUC: The area under the plasma level-time curve that gives a measure of the extent of absorption or the amount of drug that reaches the systemic circulation.

Bioequivalence studies:

It is a relative term which denotes that the drug substances in two or more identical dosage forms, reaches the systemic circulation at the same relative rate and to the same relatve extent i.e. their plasma concentration-time profiles will be identical without significant statistical differences.

Types of Bioequivalence studies:

1. In vivo
2. In vitro

In vivo Bioequivalence: The following sequence of criteria is useful in assessing the need for in vivo studies

1. Oral immediate-release products with systemic action-----
    - Indicated for serious conditions requiring assured response.
    - Narrow therapeutic margin
    - Pharmacokinetics complicated by absorption < 70% or absorption window, nonlinear kinetics, presystemic elimination > 70%.
    - Unfavourable physicochemical properities, e.g. low solubility, metastable modifications, instability etc
    - Documented evidence for bioavailability problems
2. Non-oral immediate release products
3. Modified-release products with systemic action

In vitro Bioequivalence:

1. The drug product differs only in strength of the active substances
2. The drug product has been slightly reformulated or the manufacturing method has been slightly modified by the original manufacturer in ways that can convincingly be argued to be irrelevant for the bioavailability.
3. An acceptable IVIVC and the in vitro dissolution rate of the new product is equivalent with that of the already approved medicinal product.

MICROBIOLOGY

- Edward Jenner developed vaccine against smallpox in 1798. Jenner and Pasteur gave the principle of active immunization.
- Louis Pasteur made a detailed study of fermentation in the manufacture o beer and wine.
- Penicillin was discovered by Sir Alexander Fleming.

CLASSIFICATION:

Microorganisms may have the characteristics of plant as well as animal kingdom. Because of this difficulty micro-organisms were put into separate kingdeom, *Protista*.

BACTERIA: Bacteria are microscopic rigid walled, unicellular, free living organisms without chlorophyll having either DNA or RNA. They belong to the class of Schizomycetes and Order Eubacteriales.

Shape: Bacteria commonly have following shapes and arrangements.

Coccus: These are either spherical or ellipsoidal.
Diplococci: Cocci in pair Ex: Pneumococci, Gonococci, Meningococci.
Cocci in Cluster: Ex: Staphylococcus aureus
Cocci in Chain: Streptococci lactis
Cocci in group of four: Tetrad
Cocci in Group of Eight: Sarcina

Bacilli: Bacilli are rod-shaped organism. Rods provide a higher surface area to volume ratio and hence the number of rod shaped bacteria is far greater than that of spherical acteria.

Coccibacilli: They are usually short bacilli.
Fusiform: They are bacilli tapered at both ends.
Filamentous bacilli: They are bacilie growing in long filaments.
Vibrio: They are comma shaped, curved rods ex: Vibrio cholera

Spirochaetes: They are thin, motile, spiral, flexible organisms with several spirals ex: *Treponema pallidum*
Spirilla: They are longer rigid rods with several curves o coils ex: *Spirillum minus*.

Anatomy of Bacteria: The bacterial cell consists of cytoplasm, which is enclosed within a cytoplasmic membrane and this membrane presses against at the cell wall. It contains:

Capsule: It is a gelatinous secretion of bacteria forming a thick coat around cell wall. It protects the bacterial cell against deleterious agents such as lytic enzymes.
Cytoplasmic membrane: It is 5-10 nm thick and acts as osmotic barrier. It has little strength and does not contriute to maintain cell shape. It is responsible for selective passage of food and waste materials by osmosis.
Cell Wall: It is thick, rigid and strong. Maintains shape o the cell,and it can be removed by lysozymes.
Cytoplasm: It is enclosed within the cell bound by the cell membrane. Within the cytoplasm may be located the granules, spores, vacuoles and other internal bodies.
Nucleoid: It is a long ilament of DNA tightly coiled inside the cytoplasm but not surrounded by nuclear membrane.
Flagella: The organ of locomotion in motile bacteria is flagella. They are hair like cytoplasmic appendages.
Fimbriae (Pili): They are short, very thin, filamentous, straight, hair-like attachments of the cell wall.
Mesosomes: These are used for respiration process.
Spores: Spores are highly resistant, dormant state o bacteria developed in some cels. They are resistant to heat, drying, freezing and toxic materials.

Some of common bacterial diseases:

Disease	**Causative Bacteria**
Scarlet fever	Streptococcus pyogenes
Pneumonia	Streptococcus pneumonia
Gonorrhoea	Neisseria gonorrhoeae

Diphtheria	Coryneacterium diphtheria
Tuberculosis	Mycobacterium tuberculosis
Leprosy	Mycobacterium leprae
Tetanus	Clostridium tetani
Syphilis	Treponema pallidum
Gastroenteritis	Salmonella typhimurium
Whooping cough	Haemophilus pertussis

FUNGI:

Algae and fungi are the two subdivisions of Phylum Thallophyta, which consist of most primitive plants. Algae possess chlorophyll but fungi do not. Some fungi produce toxic substances called mycotoxins. Fungi are larger in size than bacteria and have more complicated structure and reproduce both sexually and asexually.

Morphology: Two principal group of fungi are moulds and yeasts, and two sub groups are yeast like fungi and dimorphic fungi.

Moulds: They show tubular branched filaments called hyphae. The hyphae may be septate or non-septate. The hyphae intermingle to form a network called the mycelium.

True yeasts: They are round or oval, unicellular fungi with filaments and reproduce by budding.

Fungal Infections: Only about 100 species of fungi are known to cause infectious diseases in human. Infection of human usualy occurs only accidentally through contamination of cuts and arasion by soil or by inhalation of dust containing spores of conidia.

Mycoses: Theses diseases are divided into four groups.

1. Systemic/Deep mycoses: These primarily involve internal organs and viscera.
2. Subcutaneous: These involve skin, subcutaneous tissue, fascia and bone.
3. Cutaneous: These involve epidermis, hair and nails. The respective fungi are called dermatophytes and the diseases are known as dermatophytoses.

4. Superficial mycoses: These involve only hair and most superficial layer of epidermis. The superficial mycoses form the great bulk of mycotic diseases in India mostly due to T. rurum.

Disease	**Causative Fungus**
Candidiasis	Candida albicans
Coccidiodomycoses	Coccidioides immitis
Histoplasmosis	Histoplasma capsulatum
Aspergillosis	Aspergillus fumigates
Ringworm	Microsporium audouini
Athlete's foot	Epidermophyton loccosum
Barber's itch	Tricophyton species

Treatment for Fungal infections: Griseofulvin, Amphotericin, Nystatin and Flucytosin.

RICKETTSIAE

Rickettsiae are minute microorganisms having the properties between bacteria and virus. They are non-motile, non-encapsulated, don't produce spores and capsules, and look like small bacteria readily visible. They contain both DNA & RNA.

They readily cultivated in the yolk sac of developing chick embryo. Rickettsiae are sensitive to Tetracyclines and chloramphenicol.

Disease	**Causative Agent**
Epidemic typhus	**R**ickettsiae prowazeki
Murine Typhus (Endemic)	**R**. mooseri
Rocky mountain spotted fever	**R.** rickettsi
Rickettsial pox	**R.** akari
Scrub fever	**R.** tsusuga mushi
Q fever	Coxiella urnetii
Trench fever	R. quintana

CHLAMYDIAE (BEDSONIA)

Chlamydiae were considered as viruses due to their intracellular parasitism but they differ from the viruses as they possess both DNA & RNA, contain variety of enzymes, they have ribosomes, multiply by binary fission. Chlamydiae grow well in the yolk sac of embronated eggs. Mice, guinea pigs and rabbits are infected by inoculation.

Diseases of Chlamydiae: Psittacosis, Lymphogranuloma venereum and Trachoma

VIRUSES

Viruses are nucleoprotein particles capable o multiplication in certain living cells. They differ from bacteria in being intracellular obligate parasites, contain either DNA or RNA, they don't multiply by binary fission.

Structure: Simplest structure of viruses is nucleocapsid, which consists of a core of DNA or RNA encapsulated by a protein coat called a capsid. The DNA/RNA core may be a single or double stranded molecule. The protein coat forms a protective covering or the nucleic acid core. It is composed of numerous morphological subunits called capsomeres. Each capsomeres around the nucleic acid core may be arranged in isohedral cubic symmetry or helical symmetry. The term virion is applied to the complete infective virus particle.

Multiplication: Bacteria multiply by binary fission while viruses enter a living cell and mix with RNA or DNA of the cell, break up into minute particles and are lost for some time.

STAINING TECHNICHES FOR IDENTIFICATION OF BACTERIA

Bacteria are too small in size to be seen without the use o microscope. The problem is complicated because most of the bacteria are colorless and the refractive index of the protoplasm is same as that of water.

Commonly used dyes in Hanging Drop process are eosin/sodium eosinate, methylene blue, crystal violet, saranin etc.

Commonly used dyes in Simple staining are Basic dyes such as crystal violet, carbol fuschin or methylene blue.

Gram Staining: The Gram stain is the most useful and widely employed differential stain in bacteriology. It divides bacteria into two groups: Gram Positive and Gram Negative.

Gram Stain method: Prepare heat-fixed smears of microbe and place the slides on the staining rack and flood the smears with crystal violet and allow to stand for 30 seconds. Rinse with water then cover with Gram's iodine mordant and allow to stand or 1 minute and rinse with water. Declorize with 95% alcohol and rinse then counterstain with safranin for 60-80 seconds. Gram positive organisms stain blue to purple, while Gram negative organisms stain pink to red.

Acid-Fast Staining (Ziehl-Neelsen): A few species of bacteria in the genera Mycobacterium and Nocardia, do not readily stain with simple stains. These microorganisms can be stained by heating them with Carbol fuschin. The heat drives the stain into the cells. Once the microorganism have taken up the carbol fuschin, they are not easily decolorized by acid-alcohol, and hence termed acid fast.

Negative Staining: In this method bacteria are not stained hence they appear as bright objects in contrast with the stained background. Negative staining is particularly suitable for capsules, which appear as clean halo between refractile outline of cell wall are grayish background of *Indian ink*. It is achieved by mixing bacteria with an acidic stain such as nigrosin, Indian ink or eosin. These stains either produce a deposit around the bacteria or produce a dark background so that the bacteria appear as unstained cells with a clear area around them.

Endospore Staining: The endospores are stained with Malachite green. Heat is used to provide stain penetration. The resof the cell is then decolourized and counter-stained a light red with safranin.

PATHOLOGY

Anaemias: In anaemia there is not enough Haemoglobin available to carry sufficient oxygen from lungs to supply the needs of the tissues. This is classified as:

I)Impaired Erythrocyte Productions:

a)Iron deficiencies b)Megaloblastic anaemia c)Hypoplastic anemia

II) Increased Erythrocyte Loss:

a)Haemolytic anemias b)Normocytic anemia.

Iron Deficiency Anemia: The daily requirement of iron intaken in men is 1-2mg, for women is 3mg.

Megaloblastic Anemia: Maturation of erythrocyte is impaired when deficiency of Vitamin B12/Folic acid occurs & abnormally large erythrocytes are found in blood.

Pernicious Anemia: Most common form of Vitamin B12 deficiency anemia. It is an autoimmune disease in which auto-antibodies destroy intrinsic factor and parietal cells in the stomach.

Hypoplastic & Aplastic Anemia: These are due to varying degrees of bone marrow failure. Bone marrow function is reduced in hypoplastic anemia & absent in aplastic anemia.

Haemolytic anemia: These occurs when red cells are destroyed while in circulation or are removed prematurely from circulation because the cells are abnormal or the spleen is overactive.

Sickle Cell Anemia: The abnormal haemoglobin molecule become misshapen when deoxygenated, making erythrocytes sickle shaped.

Thalassemia: There is reduced globin synthesis with reluctant reduced haemoglobin production and increased friability of cell membrane, leading to early haemolysis.

LEUCOCYTE DISORDERS:

Leucopenia: Total blood leukocyte count is less than 4000 per cubic mm.

Granulocytopenia/Neutropenia: Reduction of granulocyte (most of them are neutrophils). Extreme shortage/absence of granulocytes is called agranulocytosis. Phenylbutazone, phenothiazines, some sulphonamides can cause agranulocytosis.

Leukemia: Malignant proliferation of white blood cells precursors by bone marrow. It results in uncontrolled increase in production of leucocytes and/or their precursors.

Thrombocytopenia: Blood platelet count below 1,50,000/cubic mm.

ATHEROMA: Patchy charges develop in the tunica intima of large & medium sized arteries. These consist of accumulations of cholesterol and other lipid compounds, excess smooth muscle and fat filled monocytes.

Arteriosclerosis: This is a progressive degeneration of arterial walls, associated with ageing, accompanied by hypertension.

Aneurysms: These are abnormal local dilatations of arteries. The causes are atheroma, hypertension and defective formation of collagen in arteries.

Superficial Thrombophlebitis: A thrombus forms in a superficial vein and the tissue around the affected vein becomes red and painful.

Deep Vein Thrombosis (DVT): A thrombus form in deep vein commonly in the lower limb, pelvic or iliac veins but occasionally in an upper limb. The thrombus effects long section of vein and leads to fibrinolysis.

Varicose Veins: A varicose vein is one which is so dilated that the valves do not close to prevent backward flow of blood. Such veins lose their elasticity, become elongated & tortuous and fibrous tissue replaces the tunica media.

Hemorrhoids: Sustained pressure on the veins at the junction of the rectum and anus leads to increased venous pressure, valvular incompetence and the development of hemorrhoids.

Ischemic Heart Disease: This is due to the effects of atheroma, causing narrowing or occlusion of one/more branches of coronary arteries. The narrowing is caused by atheromatous plaques.

Angina Pectoris: Increased cardiac output require during extra physical effort causes severe ischemic pain in the chest.

Rheumatic Heart Disease: Rheumatic fever, caused by streptococcus pyogenes. The antibodies developed to combat the infection, may damage heart.

Increased Intracranial Pressure: The cranium forms a rigid cavity enclosing the brain, cerebral blood vessels, blood and Cerebrospinal fluid. An increase in volume of any one of these will lead to raised intracranial pressure. The effects of increased Intracranial pressure are: displacement of brain, obstruction of the flow of Cerebrospinal fluid, Vascular damage, Neural damage, Bone charges.

DEMENTIA: Dementia is caused by progressive, irreversible degeneral and atrophy of cerebral cortex and results in mental deterioration. There is gradual impairment of memory, intellect and reasoning.
a)*Alzheimer's Disease*: It is of unknown aetiology although genetic factors may be involved. There is progressive atrophy of the cerebral cortex accompanied by deteriorating mental functioning.

b)Huntington's Disease: It is caused by genetically abnormal persons with deficient production of neurotransmitter GABA. Extrapyramidal changes causes chorea, rapid uncoordinated jerking movement of limbs and involuntary twitching of facial muscles.

Parkinson's Disease: In this disease, there is gradual degeneration of dopamine releasing neurons in extrapyramidal system. This leads to lack of control and coordination o muscle movement.

Multiple Sclerosis: In this disease, there are areas of demyelinated white matter, called plaques, irregularly disturbed throughout the brain and spinal cord, grey matter in the brain and spinal cord may also be affected because of arrangement of satellite oligodendrocytes round cell bodies. In the early stages there may be little damage to axons. Effects of Multiple sclerosis: weakening of skeletal muscle & sometime paralysis, lack of coordination & movement, disturbed sensation ex: burning or pin & needles, incontinence of urine, visual disturbance especially blurring and double vision.

Phenylketoneuria: There is a genetic disorder in which the gene needed for synthesizing the enzyme phenylalanine hydroxylase is absent. This enzyme normally converts phenylalanine to tyrosine in the liver. Phenylalanine is intermediate metabolite that accumulate in liver cells and overflows into the blood. In high quantities, it is toxic to nervous system and if untreated this condition results in brain damage & mental retardation within a few months. Tyrosine is a constitute of skin pigment melatonin and depigmentation occurs: affected children are air skinned and blonde.

Rheumatic Arthritis: This is chronic progressive inflammatory autoimmune disease. It is systemic disorder where inflammatory changes not only affect synovial joints but also heart, blood vessels and skin. Development of auto immunity may be initiated by microbial infection.

GOUT: It is caused by development of sodium urate crystals in joints and tendons that provokes an acute inflammatory response. It occurs in some people whose

blood uric acid is abnormally high due to either over production or defective excretion by the kidneys. Uric acid is a waste product of breakdown of nucleic acids ie. DNA & RNA and is produce in excess when there is large scale cell destruction. In many cases only one joint is involved and it is typically red, hot and painful. The sites most commonly affected are metatorsopharyngeal joint of big toe and the ankle knee, wrist and elbow joints.

COMMUNICALE DISEASES

Chicken Pox (Variecella) : It is mild, acute communicable viral infection affects children under 10 years age. It is characterized by vesicular skin rash along with fever and malaise caused by Varicccells Zoster. It is airborne disease transmitted by droplet infection. The virus can cross the placental barrier and infect the fetus (Congenital varicella). As per IP 2007, Varicella vaccine is a freeze-dried preparation of Herpesvirus varicellae. The vaccine does not provide life-long protection, and second dose is needed. Calamine lotion is applied locally because it is a topical barrier preparation.

Measles (Rubeola): Measles is caused by RNA Paramyxo virus and is characterized by fever, catarrhal symptoms of upper respiratory tract and red eye, known as Cough, Coryza (runny nose), and conjunctivitis followed by maculopopular erythematous rashes. Transmission occurs by droplet infection. Most patients recover without specific treatment. MMR vaccination will effectively control the infection.

Influenza (Flu): Influenza is acute infection of respiratory tract and characterized by abrupt onset fever, headache, chills and sore throat, cough without sputum, weakness and severe aches and pains in the back and limbs. It is caused by RNA viruses belong to myxoviruses. Prophylactic immunization is best approach. Killed virus vaccines (Inactivated influenza vaccine) is used. Neuraminidase inhibitors such as Tamiflu or Relenza have been found.

Swineflu: It is caused by Influenza A or H1N1 virus. Tamiflu can be used.

Diphtheria: It is caused by corynebacterium diphtheria, a rod shaped Gram positive bacteria. It is localized in throat, nose and tonsils, characterized by involvement of respiratory system and formation of false membrane for a soluble exotoxin. Peculiar inflammation of the surface membrane to the nose, throat and tonsils occur. Prevention is artificial active immunization with alum precipitated diphtheria toxoid. The commonly used vaccine is DPT which protects from Diphtheria, Pertussis and tetanus. Treatment consists of anti-diphtheria serum, antibiotics and relief of symptoms. 1 Lakh units of Penicillin in normal saline can be injected 3 hourly or 2-3 days.

Whooping Cough (Pertussis): It is caused by Haemophilus pertussis. An acute respiratory infection involving the trachea, bronchi and bronchioles. The disease develops slowy with fever, cold and an irritating cough. The child then becomes more ill and suffers rom the typical cough with the characteristic whoop. Active immunization of all infants with triple vaccine is preventive measure. Antibiotics such as erythromycin may help in alleviating symptoms quickly.

TUBERCULOSIS: TB is a specific communicale disease caused by Mycobacterium tuberculosis, it primarily afects lungs and causes pulmonary TB. It can also affect intestine, meninges, bones & joints, lymph nodes skin and other tissues of the body. Cough is the earlier symptoms, fever continues for a long time. Pain in the chest, feeling of weakness and loss of weight are associated symptoms. Blood in sputum appears in later stage.

Diagnostic Tests for TB: Tuberculin skin test, Bronchoscopy, Chest CT scan, Interferon Gamma blood test such as QuantiFeron-TB Gold Test, sputum examination for cultures.

Treatment: First line drugs Isoniazid, Rifampicin, Pyrazinamide, Ethambutol, Second line choice drugs are Amikacin, Streptomycin, Para amino salicylic acid and Ethionamide. Bedaquiline is used or MDR-TB.

POLIO: Polio is caused y poliovirus which affecting the Central Nervous System and infrequently resulting in paralysis o voluntary muscles of lower extremities. The attack begins with ever, headache, vomiting, pain and stiffness of the neck,

sometimes convulsions followed by paralysis of limb. No treatment available, vaccination is preventive measure.

HEPATITIS: It is characterized by inflammation of liver cells. The disease may also be autoimmune. Hepatitis A infection is an acute infectious disease characterized by jaundice. It is spread by faeco-oral route. Contamination water & food may lead to explosive outbreaks. Active immunization is preventable measure.

CHOLERA: Cholera is caused by Gram Negative, non motive bacteria Vibrio cholera. It is acute specific infection of gastro-intestinal tract. It is characterized by sudden onset of severe watery diarrhea, vomiting resulting an extreme dehydration, low BP and collapse. Cholera vaccination used for immunization. Treatment consists of rehydration and antibiotics. Tetracyclines and chloramphenicol in doses of 500 mg o either drug 4 times a day is recommended for 3 days. Furalizine & septran are also recommended for containment of cholera.

TYPHOID: Typhoid is caused by Salmonella typhi, is an acute communicable disease characterized by a typical continuous fever for 3-4 days, relative bradycardia with involvement of lymphoid tissues and considerable constitutional symptoms. Widal test is used to diagnose typhoid. 3rd generation cephalosporins like Ceftriaxone, Cefotaxime, Cefixime are treatment of choice. Ciprofloxacin, Ofloxacin may be used as first choice drug if resistance is uncommon.

FOOD POISONING: Food poisoning is an acute gastroenteritis acquired through ingestion of contaminated and injurious food or drinks. Bacterial food poisoning is caused by ingestion of food contaminated by living bacteria or their toxins.

i)*Salmonellosis*: Caused by Salmonella typhimurium, Salmonella entericides and Salmonella cholersuis. The causative organism multiplies in intestine causing acute enteritis and colitis. The onset is sudden with chills, fever, nausea, vomiting and a profuse watery diarrhea lasting for 2-3 days.

ii)*Staphylococcal food poisoning*: It is caused by enterotoxins of Staphylococcus aureus. Toxins act directly on intestine and CNS. Fever is rare.

iii)*Botulism*: It is caused by exotoxin of Clostridium botulinum usually found in under processed food. It enters the food as spores. Home preserved foods, smoked or pickled fish, home-made cheese and similar low acid foods are chief sources of botulism. It is characterized by dyspepsia, diplopia, dysarthria, blurring of vision, muscle weakness. Antitoxin acts as prophylactic against botulism. Guanidine HCL 15-40 mg/kg body weight can be given orally.

HOOKWORM INFESTATION: Hookworm lives in the small intestine as a parasite. The eggs are excreted in the stools and develop into larvae in a warm moist soil. Whenever in contact with human skin they penetrate it and are carried to lungs and go up the air passages and windpipe and finally swallowed. Two species of hookworms are Anchylostoma duodenale and Necator americanus. Hookworm infestation causes severe anemia, joint pains, dyspepsia, oedema and eosinophelia. Treatment: Benzimidazoles like Albendazole, Mebendazole are common drugs act by binding to nematode's beta-tubulin and subsequently inhibiting microtubule polymerization within the parasite. Levamisole and Pyrantel pamoate may be used.

PLAGUE: Plague is caused by Pasturella pestis, a Gram negative non motile cocco bacilli, is a highly infectious disease transmitted to man by infected rat flea. It is characterized by high fever, inflammation of lymphatic glands, forming buboes and sometimes by pneumonia or septicemia. The lymph nodes swell rapidly to the size o hen's egg or larger. They are painul and are called *buboes*. Patient affected with rigor, headache, bodyache, cough with expectoration and pain in chest. Patient suffers from breathlessness.

Human plague is of three varieties.

Bubonic Plague: There is fever, prostration with inflammation of regional lymph glands commonly those in groin, axilla and neck, when buboes are formed.

Pneumonic plague: It is spread by droplet infection from man to man and does not spread through rat fleas.

Septicemia plague: The blood infection occurs without the formation of buboes. It is rare and but usually fatal.

Treatment: Antibiotics like Streptomycin, Gentamicin, Doxycyline or Ciprofloxacin are used to treat plague.

Malaria: Malaria is caused by protozoal infection by Plasmodium vivax, P falciparum, P malariae and P ovale. Malaria is transmitted through Anopheles mosquitoes. Malaria parasite enter into human through Sprozoites. It is characterized by extreme cold lasting for 15-60 minutes, patient feeling burning hot and intense headache, temperature shooting up to 106°C.

Treatment: Chloroquine is often used as an anti-malarial medication. Combination of Quinidine or Quinine + Doxycyline/Tetracycline+Clindamycin **OR** Atovaquone + Proguanil, Mefloquine or Artesunate, Combination of Pyrimethamine with Sulfadoxine.

FILARIASIS: Filariasis mainly affected by Wucheraria bancrofti. Filariasis mainly affects the lymphatic system. The disease is transmitted by culex, Mansonides mosquitoes. Diethylcarbamazine (Hetrazon) is the only drug available against Filariasis. Albendazole combined with Ivermectin is treatment of choice. Comination of Diethylcaramazine with Albendazole is also effective. All these treatments are microilaricides but no effect on adult worms.

RABIES: It is acute viral infectious disease of nervous system transmitted by rabid dogs. Important characteristic of disease is Hydrophobia. It is caused by neurotropic RNA virus of Rhabdo virus. When dog bite, the would should be washed with soap and water, cauterized with carbolic acid, permanganate crystals or pure nitric acid.

Anti Rabies Vaccine is a nerve tissue vaccine prepared from the brain of adult sheep or goat and inactived y phenol, BPL vaccine is β-propiolactone inactivated duck embyo vaccine and Human Diploid Cell Tissue Culture Vaccine (HDCV) inactived by BPL also available.

TRACHOMA: Trachoma is an infectious disease of the eye characterized by inflammation o conjunctiva and cornea. It is one of main causes of blindness in India. It is caused by Chlamydiae trachomatis, which invades mucous membrane covering the surface of the eye ball and lining of the lids.

Sulphacetamide eye drops, Tetracycline eye ointment are used in treatment of trachoma. Erythromycin and Rifamycin also used for treatment.

TETANUS: It is characterized by painful spasms and twitching of the jaw muscles. This causes difficulty in opening of mouth and in mastication. Contraction of muscles of the neck and trunk makes the neck rigid. Tetanus is caused by exotoxins of Clostridium tetani.

Passive immunization is carried out with Anti Tetanus Serum (ATS) or Human Tetanus Immunoglobulin. Penicillin and Tetracycline are also given to injured persons as these antibiotics kill the tetanus bacilli.

LEPROSY: Leprosy is a chronic infectious disease characterized by lesions of the skin and by involvement of peripheral nerves with consequent anesthesia, muscle weakness, paralysis and trophic changes in the skin, muscles and small bones of hands and feet. Leprosy is caused by Mycobacterium leprae. Dapsone, Rifampicin, Cloazimine, Fluoroquinolines, Macrolides, Minocyclines are used for treatment.

SYPHILIS: Syphilis is caused by Treponema pallidum, a spiral shaped bacterium. It is not only medical problem but also social & psychological one. The disease ultimately result in serious complications such as enlargement of heart & blood vessels, blindness, deafness, paralysis, insanity & sterility.

Penicillin is the drug of choice. Azithromycin is first choice treatment. 3rd generation cephalosporins ceftriaxone is equally effective.

GONORRHEA: It is characterized by inflammation of urethra, painful micturition, purulent discharge and liability to certain complications such as ophthalmia, endocarditis and arthritis. It is caused by Neisseria gonorrhoeae, a Gram negative intracellular diplo-coccus.

Treatment should be: Benzyl penicillin (5 Million units) with 1-2 gm of Probenecid OR Procaine Penicillin with 1-2 gm Probenecid and Ampicillins 3-5 gm of single dose plus 1-2 gm of probenecid.

IMMUNE SYSTEM

The organs of the immune systems are known as lymphoid organs since they are residence of key cells of immune system i.e. lymphocytes. Essentially antibodies are immunoglobulins produced by mature B cells in response to antigen. Antibody is made of two heavy chains and two light chains. The variable region, which differs from one antibody to another, allows an antibody to recognize its matching antigen.

IgG: Antibody that works efficiently to coat microbes, speeding their uptake y other cells in the immune system.

IgM: Very effective in killing bacteria.

IgA: Concentrate in body fluids such as tears, saliva, and the secretions of the respiratory and digestive tracts, which guard the entrances to the body.

IgE: Mainly they protect against parasitic infections and are responsible for the symptoms of the allergy.

IgD: Remain attached to B cells and play a key role in initiating early B cell responses.

PHARMACEUTICAL CHEMISTRY

ANTIOXIDANTS

Sulphur Dioxide: Used in lotions, SO_2 along with glycerine is used to cure sore throat, in cold, tonsillitis and skin infections.

Disadvantage: inhalation results in irritation o respiratory tract which may lead to bronchoconstriction, pulmonary edema.

$NaHSO_3$ (Sodium bisulphite): Antiseptic,in parasitic skin diseases, to stabilize kidney stones, in injections of epinephrine.

$Na_2S_2O_5$ (Sodium metabisulphite): To stabilize injections of adrenaline, apomorphine.

$Na_2S_2O_3$ (Sodium thiosulphate): Antidote in treatment of cyanide poisoning along with $NaNO_2$. Antifungal, used in treatment of pityriasis versicolor.

GASTROINTESTINAL AGENTS

Acidifying agents: used in achlorhydria ex. NH_4Cl, NH_4NO_3, $CaCl_2$

ANTACIDS: Every antacid product must have a total neutralizing capacity of at least 5 mEq of HCl/dosage unit. Antacids should not given with Tetracyclines.

Two types of Antacids:

1. Systemic (Absorbable) : $NaHCO_3$
2. Non Systemic (Non absorbable): Al salts, Mg salts, $CaCO_3$,Sodium carboxy methyl cellulose

Dried Aluminium hydroxide Gel: It is used as phosphate binder in patients with chronic renal failure, and is used as an adjuvant in manufacture of adsorbed vaccine.

$CaCO_3$: These are given with Mg antacid due to Calcium's constipation effect. The liberation of CO_2 may discomfort in patients.

MgO: It is used as Osmotic laxative property.

$NaHCO_3$: Electrolyte replenisher, systemic alkalining agent. Used in treatment of acute poisoning by acidic drugs like (salicylates, phenobarbitone), Used in eye lotions to aid remove of crusts in Blepheritis, Used as in ear drops, to soften & remove ear wax. Disadvantages are stomach cramps, flatulence, vertigo.

Combinations:

Algicon Tablets: $Al(OH)_3$ + $MgCO_3$ + Mg Alginate + $MgCO_3$ + $KHCO_3$
Simeco Tablets: $Al(OH)_3$ + $MgCO_3$ + $Mg(OH)_2$ + Activated dimethicone
Magaldrate: (28-39%) MgO + (17-25%) Al_2O_3

PROTECTIVES & ADSORBENTS

These are used for treatment of diarrhea. They adsorb toxin, bacteria and provide coating to mucosal layer.

Bismuth Subcarbonate: antacid, dusting powder, protective.

Kaoline: Adsorbent, antidiarrhoeal.

SALINE CATHERTICS

These are also called purgatives, which fastens and increase evacuation of feacal matter from bowles.

Laxative: Mild cathertics used for short term therapy. Laxatives are four types, (i) stimulant (ii) Bulk forming (iii) Emollient (iv) Saline

Stimulants: These act by local irritation of intestinal tract increasing peristaltic activity. Ex Aloin, Cascara, Rhubarb, Senna, Castor oil.

Bulk Forming: Swell when moistened, increasing bulk , stimulate peristalsis. Ex: Psyllium seeds,methyl cellulose, Sodium carboxy methyl cellulose, Karaya gum.

Emollient: Stool softene or lubricants. Ex: Mineral oil, d-octyl Na sulphosuccinate (anionic surface active agent).

Saline laxative: $MgSO_4$, Milk of Magnesia, Mg stearate, K & Na tartrate.

$MgSO_4$: Saline laxative, used to control seizures, hypothyroidism, used in eclampsia (Convulsions in pregnancy).

TOPICAL AGENTS

Protectives:

Bentonite: Stailizing agent, and adsorbent.

Calamine: Used in urticaria (Skin eruptions), eczema and in sunburn. Calamine lotion: Calamine + ZnO + Bentonite.

Silicone polymers (Dimethicone): These are used as water repellants, used in barrier creams for protecting skin against water-soluble irritants, used in bedsores, napkin rashes. These also used for treatment of flatulence.

Talc:

TiO_2: Mild astringent, protective application in eczema. It is used for relief of pruritis, and used to prevent sunburn.

ZnO: Astringent, as a soothing & Protective application in eczema. It is used to prevent sunburn, in treatment o skin ulcerations.

Zn stearate: Mild astringent, antimicrobial properties, soothing and protective agent in skin inflammation.

ANTIMICROBIALS

Borax:

Chlorinated Lime (Bleaching powder): used in swimming pools, chlorination for disinfectant feces, urine. It is used as a cleansing agent for lavatories, drains, in preparation of surgical chlorinated soda solution (Dakin's solution).

H_2O_2: Disinfectant, anti-infective. Kills bacteria including E. Coli, Staphylococcus, typhoid bacilli.

I_2: Lugol's Solution (strong Iodine solution) is the only official solution of Iodine that contains no alcohol. It is used or internal administration as counter irritant and disinfectant.

Weak Iodine solution: I_2 + KI

Iodine Tincture: I_2 + NaI + small amount of alcohol

Phenolated Iodine solution (Binlton's solution): It is used as antihyperthyroid agent, topical anti-infective, germicide.

Povidone-Iodine: Complex of Iodine with povidone. Antiseptic for treatment of contaminated wounds, used in gargles and mouthwashes.

Hg: disinfectant, parasiticide, and fungicide.

Ammoniated Mercuric acid: It is used in eye ointments for local treatment of minor infections, eradication of crab lice from eye lashes, inflammation of eye.

$KMnO_4$: Astringent, anti-infective & Bactericidal. Solution is used to clean ulcers/abscess, as wet dressing in baths in eczematous conditions. Solutions have also used in bromhidrosis (evil smelling persperiation). It is used in mycotic inflammation such as athlet's foot, in poison ivy dermatitis, stomach washout in treatment of poison by morphine, opium.

$AgNO_3$: Disinfectant, Astringent, irritant properties. Used to destroy warts & other skin growths.

ASTRINGENTS

Dilute solution of metal cation has surface protein precipitant activity on tissue is called astringent.

Alum: a powerful topical astringent, used as haemostatic agent, used in mouth washes, gargles.

$ZnSO_4$: To treat conditions associated with Zn deficiency like acrodermatitis enteropathica.

Selenium sulphide: Antifungal, antiseborrhoeic activities, used in shampoos & in lotions.

RESPIRATORY STIMULANTS

Ammonium Carbonate:

Expectorants: Reduce viscosity of mucous and increase secretion of respiratory tract. Ex NH_4Cl, Na citrate, KI.

Bronchodilators: It is used in cough associated bronchospasm. Ex; Ephedrine

Antitussives: Act on cough center. Ex; Codeine.

Mucolytics: Liquefy mucoprulent/tenacious sputum. Ex; Acetylcysteine.

Terpene hydrate: Direct effect on bronchial secretory cells.

EMETICS

Centrally acting: Morphine

Peripherally acting: Ex Mustard, antimony & K tartrate, NaCl

Peripherally & Centrally acting: Ex Ipecacuanha

NH_4Cl: expectorant, diuretic and systemic acidifying agent.

Antimony K tartrate: It is used in cutaneous leishmaniosis.

KI: Antifungal, antitussive, expectorant agent.

ANTIDOTES

Chemical antidotes: Sodium thiosulphate, Na-Ca edentate for heavy metal poisoning.

Physiological antidote: $NaNO_2$

Mechanical antidote: Activated charcoal, $CuSO_4$, $MgSO_4$, Na_2HPO_3

ELECTROLYTES

Calcium: Constituent of bones and teeth, important function of muscle and blood clot.

Magnesium: Second most cation in concentration in intracellular fluid compartment, important in protein synthesis, in neuromuscular functioning.

Sodium: Principal cation in extracellular fluid compartment. Important in muscle contraction, nerve impulse etc.

NaCl: Used in eye drops (irritating agent), as nasal drops (to relieve nasal decongestion), as a mouth wash (to remove debris for throat infection).

KCl: in familial paralysis, myasthenia gravis (muscle weakness); Menier's syndrome (disease of inner ear), as antidote in digitalis intoxication.

$CaCl_2$: Calcium replenisher, antiallergic, urinary acidifier, anhydrous $CaCl_2$ used as a dessicant.

$FeSO_4$: Haematinic agent.

RADIOPHARMACEUTICALS

Radioactive compounds are used in medicine as source o radiation for radiotherapy and for diagnostic purposes.

Isotopes: Nuclides with same atomic number but different mass number.

- The units of Radioactivity are: Curie, Becquarel, Electron volt, Roentgen, Rad, Rem.

Three types of emission from radioactive substances are: α, β and ϒ.

- Beta radiation is used to treat surface lesions.
- Gamma radiation is used to treat deep-seated tumors
- X radiation is used to treat external therapy.

Geiger-Mueller counter is used to measure Beta and Gamma emissions.

IUPAC NAMES of Some Medicinal Drugs:

Sulfadiazine	4-Amino-N-2-pyrimidinyl benzene sulphonamide
Dapsone	4,4'-sulonyl bisbenzene amine
Isoniazid	4-pyridine carboxylic acid hydrazide/ Isoniconic acid hydrazide
Ethambutol	2,2'-(1,2-Ethanediyl diamino)bis-1-butanol
Cycloserine	D-4-amino-3-isozolidinone
Pyrazinamide	Pyrazine-2-caroxamide
Metronidazole	2-methyl-5-nitroimidazole-1-ethanol
Benzyl Penicillin	3,3-Dimethyl-7-oxy-[6(phenylacetyl)amino]-4-thia -1-azaicydo [3,2,0]heptanes-2-carboxylic acid
Quinine	6'-Methoxy cinchona-9-ol
Chloroquine	N14-(7-chloro-4-quiniolinyl)-N,N'-diethyl-1,4-pentanediamine
Chlorpromazine	2-chloro, N,N-dimethyl-10H-phenothiazin-10-propaneamine
Chlordiazepoxide	7-Chloro-N-methyl-5-phenyl-3H-1,4-benzodiazepin -2-amine 4-oxide

Diazepam	7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzenediazepine-2-one
Phenobarbitone	5-Ethyl-5-Phenyl-2,4,6-[1H,3H,5H]-Pyrimidine trione
Thiopental	5-Ehyldihydro-5-[1-methylbutyl]-2-thioxo-4,6-(1H,5H)-pyrimidine dione
Lignocaine	2-(diethylamino)-N-(2,6-dimethyl phenyl) acetamide
Adrenaline	4[1-hydroxy-2-(methylamino)ethyl]-1,2-benzenediol
Noradrenaline	4-(2-admino-1-hydroxylethyl)-1,2-benzenediol
Isoprenaline	4-(1-hydroxy-2-[1-methylethyl]-amino ethyl)-1,2 – benzenediol
Phenylephrine	(R)-3-hydroxy-α-[methylamino)methyl] benzene methanol
Salbutamol	α1-[((1,1-dimethylethyl)amino)methyl] 4-hydroxy-13-benzene dimethanol
Propranolol	1[(1-methylethyl) amino]-3-(1-napthalenyloxy)-2-propranolol
Atropine	α-[Hydroxymethyl]-benzeneacetic acid-8-methyl-8-azabicyclo[3,2,1]oct-3-ylester
Chlorothiazide	6-chloro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide
Chlorpropamide	4-chloro-N[(propylamino)carboxyl]benzene – sulphonamide
Metformin	N,N-Dimethyl imidocaron imidic diamide
Histamine	1H-Imidazole-4-ethenamine
Diphylhydramine	2-diphenylmethoxy- N,N-dimethylethanamine
Promethazine	N,N-α-trimethyl-10H-phenothiazine-10-ethenamine
Cyproheptadine	4-[5-H-Dienzo(a,b)cyclohepten-5-ylidone]-1-methyl piperidine
Pheniramine	N,N-Dimethyl-ϒ-phenyl(2-pyridine)-propanamine
Morphine	7,8-didehydro-4,5-epoxy-17-methyl morphinan-3,6-diol
Aspirin	Acetyl salicylic acid/2-(Acetyloxy)benzoic acid
Paracetamol	N-(4-hydroxy phenyl)acetamide
Indomethacin	1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetic acid
Phenylutazone	4-Butyl-1,2-diphenyl-3,5-pyrazolidinedione
Ibuprofen	α-methyl-4-(2-methylpropyl) benzene acetic acid
Ethosuximide	3-Ethyl-3-methyl-2,5-pyrrolidine dione
Procainamide	4-Amino-N[2-(diethyl amine)ethyl] benzamide

Betamethasone	7-Fluoro-11,17,21-trihydroxy-16-methylpregna -1,4-diene-3,20-dione
Cortisone	17α,21- dihydroxy, 4-pregnene-3,11,20-trione
Prednisolone	11,17,21-trihydroxy pregna-1,4-diene-3,20-dione
Progesterone	Pregn-4-ene-3,20-dione
Testosterone	17β-Hydroxyandrost-4en-3-one

PHARMACEUTICAL LAW

- Drugs & Cosmetics Act – 1940
- Pharmacy Act – 1948
- Patent Act – 1970
- Poisonous Act – 1919
- Drugs Price Control Order – 1995
- Narcotics & Psychotropic Substances Act – 1985
- AICTE – 1994
- Drugs & Magic Remedies Act – 1954
- The Medical termination & Pregnancy Act – 1971
- The Factories Act – 1949

Misbranded Drug: If it so colored, coated, powdered or polished that damage is concealed or if it is made to appear better or or greater therapeutic value than it really is **OR** if it is not labelled in prescribed manner **OR** if its label or container or anything accompanying the drug bears any statement, design or device which is false/misleading in any particular.

ADULTERATED DRUGS: If it consists, in whole or in part of any filthy, putrified or decomposed substance **OR** if it has been prepared, packed or stored under insanity condition whereby it may have been rendered injurious to health

SPURIOUS DRUGS: If it is manufactured under the name of other drug OR if it has been substituted wholly or in part by another drug or substance.

DTAB: Drug Technical Advisory Board. It consists 18 Memers.

I)Ex-Officio Members: 8

- Chairman, Director General Health Services
- Drug Controller of India
- Director, Central Drug Laboratory Calcutta
- Director, Central Research Institute Kasauli
- Director, Indian Vetarinary Research Institute
- President, Pharmacy Council of India
- President, Medical Council of India
- Director, Central Drug Research Institute

II)Elected Members – 5

- A Teacher in Pharmacy/Pharmaceutical chemistry or Pharmacognosy on the staff of Indian Universities
- A Teacher in Medicinal therapeutics of the staff of Indian Univ
- 1 Pharmacologist elected by ICMR
- 1 person elected by council of central medical association
- 1 person elected by council of Indian Pharmaceutical Association.

III) Nominated Members – 5

- 2 Persons by central govt amongst persons who are incharge of drug controller of states
- 1 person from pharmaceutical industry
- 2 government analysts.

SCHEDULES TO THE PHARMACY ACT:

First Schedule: Names of books under Ayurvedic, Siddha, Unani Tibb system.

Second Schedule: Standards to be compiled with by imported by drugs manufactured for sale, sold, stocked or exhibited for sale or distributed.

Schedules:

A – Proforma or application for licences, issues and renewal of licenses, for sending memoranda under the act.

B – Fee for analysis of drugs/cosmetics that have to be paid to central drug labs/other drug labs

C – List of biological & immunological products, antibiotic, ophthalmic, lotions, ointments & all products for parenteral use.

D – Exemptions that have been granted to drugs & importers of drugs from complying with the requirement of import of drugs & also the condition for such exemptions.

E – List of poison for which labeling and other requirement to be complied with

F - Manufacturing, testing & labeling of biological products for human use like sera & vaccines.

F(I) – Manufacturing, testing & labeling of veterinary biological

F(II) – Standard for surgical dressings

F(III) - Standard or umbellical tapes

FF – Standards for Ophthalmic preparations

G – List of substances that are require to be used under only medical supervision & which are to be labeled accordingly.

H – List of prescribed drugs

J – Diseases/ailments which a drug may not purport to prevent/cure

K – Drugs exempted from certain provisions relating to manufacture of drugs

M – GMP Requirement for factory premises, plants & equipments.

N – List of minimum equipment for efficient running of pharmacy

O – Standard or disinfectant fluids

P – Life period of drugs

P(I) – Pack size o the drugs

Q – Part I: List of dyes, colors & pigment permitted in cosmetics & soaps

Part II: List of colors permitted in soaps

R - Standard for Medical Devices

R(I) – Standard for cosmetics

S – Standard or cosmetics

T – Requirement for factory premises & hygienic condition for Ayurvedic & Unani drugs

U – Particulars to be shown in manufacturing, raw material & analytical record of the drugs

U(I) – Particulars to be shown in manufacturing, raw material for cosmetics

V – Standard for patent/proprietary medicine

W – Drugs marketed under genetic names only.

X – Names of Narcotic & Psychotropic drugs or which special control measure have been laid down

Y – Requirement & guidelines on clinical trials for import & manufacture of new drugs.

TYPES OF LICENCE:

FORMS	Guidelines
Form 19	Application which has to be made or grant/renewal of sale license by retail or wholesale to state licensing authority
Form 20	License granted to sell by retail drugs,

	drugs other than Schedule C & C(1)
Form 20 B	License granted to sell by wholesale drugs, drugs other than Schedule C & C(1)
Form 21	Licence granted to sell by retail drugs, drugs specified in Schedule C, C(1)
Form 21B	Licence granted to sell by wholesale drugs, drugs specified in Schedule C, C(1)
Form 24	Application which has to be made for grant/renewal of licence to manufacturing o drugs other than Schedule C, C(1) drugs
Form 27	Application which has to be made for grant/renewal of license to manufacture drugs specified in Schedule C, C(1) drugs
Form 24A	Application which has to be made for grant/renewal of a loan to manufacture of drugs other than Schedule C, C(1) drugs
Form 25	Licence granted to manufacture drugs other than Schedule C, C(1) & X drugs
Form 25A	Loan license granted to manufacture drugs other than excluding X
Form 28C	License granted to operate blood bank, for processing whole blood for component.

Pharmacy Council of India:

Members (Elected): 6 members, among whom there shall be one teacher from each subject of Pharma chem./Pharmacy/pharmacology.

Members (Nominated): 6 nominated by central Govt of whom four shall be possessing degree/diploma in Pharm chem./P practicing.

MCI: One member elected from Medical Council of India.

UGC & AICTE: One member from each body.

State Govt Nominee: One member from each state shall be registered pharmacists.

Ex-Officio Members: Director General of Health services, Drug controller of India, Director of Central Drug Laboratory.

STATE PHARMACY COUNCIL:

Members (elected): 6 members elected amongst themselves by registered pharmacists of state.

Members (Nominated): Five members nominated by state govt of whom at least three person possessing: degree or diploma in pharmacy/pharm chemistry.

MCI: One member elected by State medical council.

Ex-Officio Members: Chief Administrative medical officer of state, the officer incharge of drugs controllers organization of state, Government analyst.

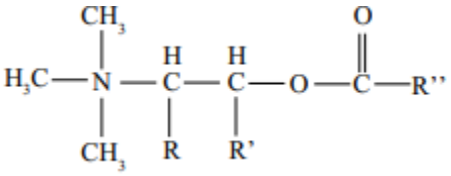
MEDICINAL CHEMISTRY

Cholinergic drugs:

Chloinergic agonist classification:

1. **Choline ester derivatives :**

General structure:



S.NO.	Name of the drug	R	R’	R”	Characteristics
1.	Acetylcholine	H	H	CH_3	
2.	Methacholine	CH_3	H	CH_3	S form is active
3.	Bethacholine	H	CH_3	NH_2	Use in hypotenia
4.	Carbachol	H	H	NH_2	Used in glaucoma.

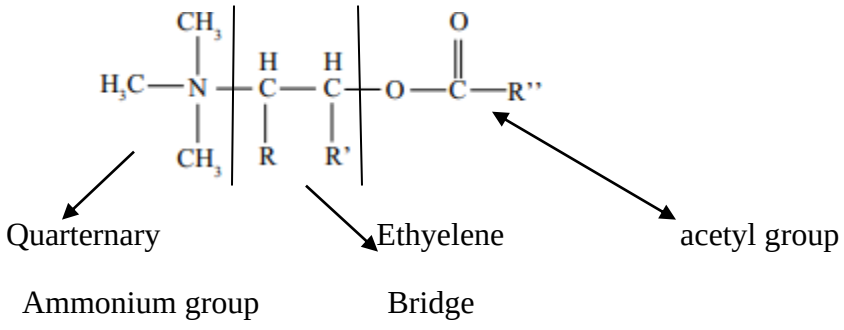
Synthesis of Acetylcholine :

Acetylcholine is synthesized from the acetyl co-enzyme A and choline by the enzyme choline acyl transferase.

Acetate + ATP + Co-A ⟶ Acetyl Co A

Acetyl Co A + Choline ⟶ Acetyl choline

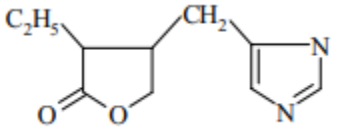
Structural Activity relation ship:



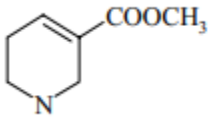
1. Any change in the ethylene bridge may affect the chemical stability of acetyl choline molecule.
2. A cationic ammonium group is essential for the manifestation of both muscarinic and nicotinic receptor activities. If one or more of the methyl groups on nitrogen atom are replaced by hydrogen or ethyl group both activities are reduced.
3. The quaternary nitrogen atom itself may be replaced by arsenic, antimony, phosphorous or sulphur atom without the loss of all acetylcholine activities.
4. If bulky substituents are placed on the terminal C-atom of acetyl group, through a fil binding and umbrella effect these substituents block the access of aetylcholine to the receptor.This results in muscarinic activity.
5. Carbachol and acetyl-β-methylcholine are the cholinergic agonist acting chiefly at muscarinic receptors while propionylcholine and acetyl α-methylcholine act chiefly at nicotinic cholinergic receptors.

Natural alkaloids:

1. Pilocarpine: It contains imidazole and tetrahydrofuran ring, obtained from Pilocarpus jaborandi and Pilocarpus microphyllus species.

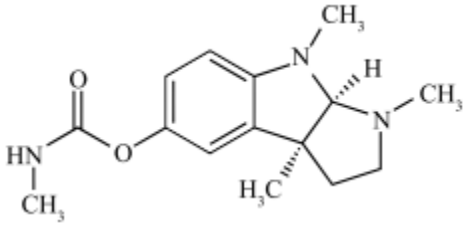


2. Arecoline: It is obtained from Areca catechu and contains 1,2,5,6-Tetrahydro Pyridine ring.



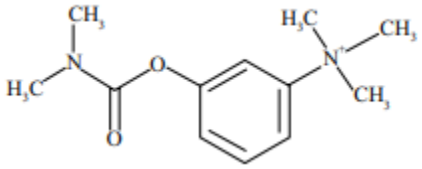
Anti cholinesterase agents:

1. Reversible
   a. Naturally occurring:
      Physostigmine: It is obtained from Physostigma venenosum It contains tertiary nitrogen which is non-polar hence becomes lipid soluble.

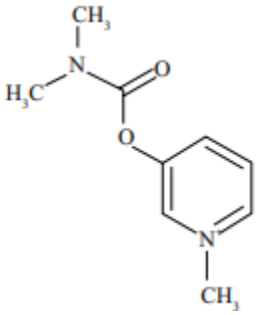


   b. Synthetic:

Neostigmine: It contains quaternary nitrogen which is made of compound hydrophilic.



Pyridostigmine:



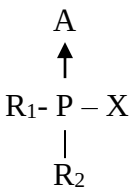
Structural activity relationship :

The two heterocyclic rings of physostigmine are not essential for anticholinesterase activity. During hydrolysis, the phenolic fragment of this drug is eliminated, leaving the carbamoyl group attached to the enzyme. The rate of hydrolysis of carbamoyl group is about 60 times less than the rate of hydrolysis of acyl group of acetylcholine.

2. **Irreversible:**
    1. Oragnophosphorous compounds:
        Parathion
        Malathion
    2. Carbamates
        Carbaryl
        Propoxur

Structural activity relationship:

1. A general formula for these compounds is as follows:



Where R_1= alkoxyl

R_2= Alkoxyl, alkyl or tertiary amine

X = A good leaving group

Eg: F, CN, Thiomalate, p-nitrophenoxy.

2. A is usually oxygen or sulphur, but many also be selenium. When A is other than oxygen, biological activation is required before compound becomes effective.
3. The R moiety imparts lipophilicity to the molecule and contributes its absorption through skin.
4. In alkoxy series, compounds which contains fluorine are more active than those containing iodine or other radical.
5. These organophosphorous compounds are nerve poisons and used as Agriculture insecticides and in the treatment of glaucoma.

Adrenergic drugs:

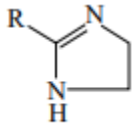
I.Directly acting Adrenergic drugs:

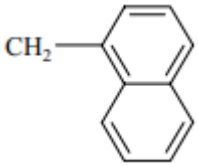
a. Selective α_1 agonist:

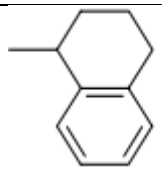
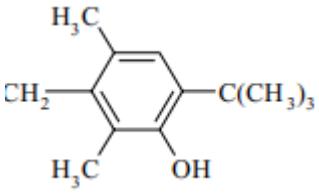
SNO.	Name of the drug	Characteristic	Side effects
1.	Phenylephrine	Used as mydriatic when cyclopegia is not require and nasal decongestant	Bradycardia
2.	Methoxyamine	Used as an nasal decongestant	Bradycardia

b. Non-selective α Agonist:

General structure:

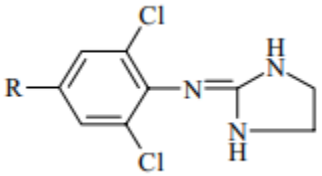


SNO.	Name of the drug	R
1.	Naphazoline	

2.	Tetrahydrozoline	
3.	Oxymetazoline	

Selective α_2 Agonist:

General structure:



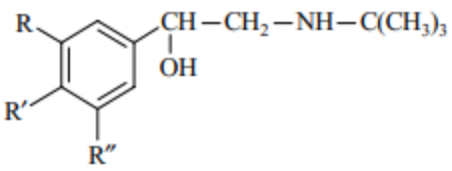
SNO.	Name of the drug	R	Characteristic
1.	Clonidine	H	Used in migraine, glaucoma.
2.	Apraclonidine	NH_2	Used in glaucoma
3.	Guanabenz	-	-

β-Agonist:

Non selective : Isoproterenol, Epinephrine

Selective β_2 agonist:

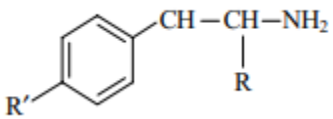
General structure:



SNO	Name of the drug	R	R'	R''
1.	Salbutamol	CH_2OH	OH	H
2.	Terbutaline	OH	H	OH
3.	Pirbuterol	CH_2OH	H	OH

Indirectly acting:

General structure:



SNO.	Name of the drug	R	R'	Uses
1.	Amphetamine	CH_3	H	It is MAO inhibitor and CNS stimulant, appetite suppressant.
2.	Hydroxyamphetamine	CH_3	OH	It gives in combination with atropine gives mydriasis.
3.	P-Tyramine	H	OH	-

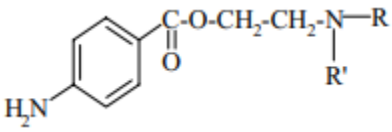
Local anasthetics:

Classification:

A. Esters:

i.Amino alkyl esters of p-amino benzoic acid:

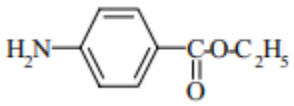
General structure:



Name of the drug	R,R'	R''''	R'''''	R''''''	
Procaine	$(C_2H_5)_2$	-	H	H	
Chlorprocaine	$(C_2H_5)_2$	-	H	Cl	
Propoxycaine	$(C_2H_5)_2$	-	H	Pro	
Tetracaine	$(CH_3)_2$	Bu	H	H	

ii. Alkylesters of amino benzoic acid:

Eg: Benzocaine



Name of the drug	C_2H_5	NH_2
Orthocaine	CH_3	OH
Butyl amino benzoate	$(CH_2)_3CH_3$	NH_2

iii. Ester of benzoic acid:

Eg: Cocaine

Piperocaine

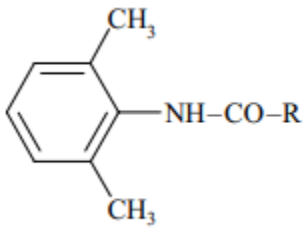
Cyclomethycaine

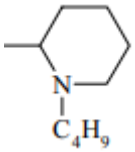
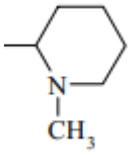
Meprylcaine

Hexylcaine

B. Amide derivatives:

General structure:



Name of the drug	Characteristic	Metabolism	Side effects	R
Lidocaine	Used in ventricular arrythmia	N-dealkylation		CH_2 –N–(C_2 H_5)$_2$
Prilocaine		N-dealkylation	Methaemoglobinemia	CH (CH_3)$_2$ –NH–C_3 H_7
Bupivacaine	Levo form is used	N-dealkylation	Cardiotoxic	
Mepivacaine		N-dealkylation		

C. Urethanes: Compounds with a “NHCOO” linkage Ex: Diperodon

D. Aminoketones:

Falicaine

Dyclone

E. Amino esters:

Ex: Dimethisoquin

Structural activity relationship for ester linkage:

a. Aryl group:

An aryl radical attached directly to the carbonyl group, results into a conjugation which in turn enhances the local anaesthetic activity.

Similarly alicyclic and aryl aliphatic carboxylic acid esters are also active local anaesthetics.

In aryl vinyl radicals (Ar - CH = CH -), the mesomeric effect of any radical does not extend to the carbonyl group and hence such compounds are not effective clinically.

The aryl substituents which increase the electron density of the carbonyl oxygen, enhances activity.

e.g., Alkoxy, amino and alkyl amino groups at ortho or para position.

b. Bridge 'X': Here the 'x' may be carbon, nitrogen, oxygen or sulphur. The nature of 'X' affects duration of action and relative toxicity.

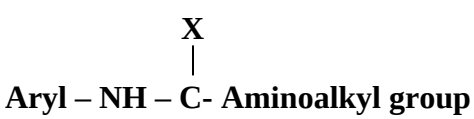
c. Aminoalkyl group:

The amino group is considered as the hydrophilic part of the molecule. The activity decreases and irritation property increases the folllwing order

$$1^{o} < 2^{o} < 3^{o}$$

The alkyl position only influence the lipid solubility.

Structural activity relationship for amide linkage:



a. Aryl group:

The alkyl substitution at Ortho or Para position, enhances the activity. It provides steric hindrance to the hydrolysis of the amide linkage and contributes to the lipid solubility of molecule.

b. Substituent:

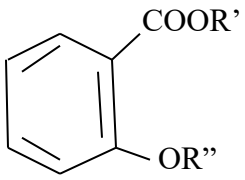
In general, X may be carbon, oxygen, or nitrogen.

NSAIDS:

It is also called as non-opioid analgesic.

Classification:

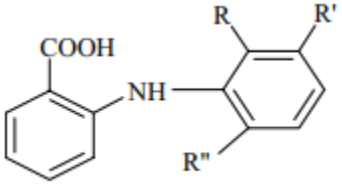
Salicylate and salicylic acid derivative:



Name	R'	R"
1. Salicylic acid	H	H
2. Methyl salicylate	CH_3	H
3. Sodium salicylate	Na^+	H
4. Phenyl salicylate	C_6H_5	H
5. Aspirin	H	$COCH_3$

N- anthralic acid derivatives:

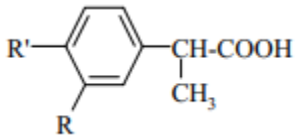
General structure:



Name	R	R’	R”	Name	R	R’	R”
Flufenamic acid Meclofenamic acid	H Cl	CF_3 CH_3	H Cl	Mefenamic acid	CH_3	CH_3	H

Aryl propionic acid derivatives:

General structure:



Name of the drug	R	R’	Side effects
Ibuprofen	H	CH_2 $CH(CH_3)_2$	Hepatotoxicity, Constipation.
Phenoprofen	O-C_6H_5	H	Antiplatelet
Ketoprofen	C=O-C_6H_5	-	-
Flurbiprofen	F	C_6H_5	-

Aryl and Hetero aryl Acetic acid derivative:

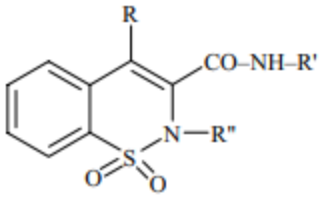
Diclofenac sodium

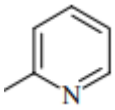
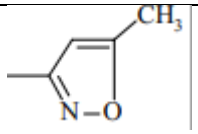
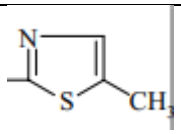
Aciclofenac

Ketorolac

Enolic acid derivatives:

General structure:



Name of the drug	R	R’	R”
Piroxicam	OH		CH_3
Isoxicam	OH		CH_3
Meloxicam	H		H

Pyrazole or Pyrazolidine derivatives:

- **A**ntipyrine
- Aminopyrine

Indole acetic acid derivatives:

Ex: Indomethacin

Sulindac

Structural activity relationship for Salicylic acid derivatives:

a. Various substitutions on the carboxyl or hydroxyl group result into change in potency as well as toxicity.
b. The ortho position of the OH group is an important feature for the action of the salicylates.
c. Benzoic acid, though much weaker, shares many of the actions of salicylic acid.

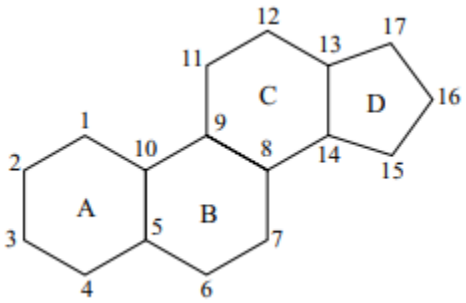
Structural activity relationship of Aryl acetic acid derivatives:

1. The following substituents generally give expected activities:
   a. Indole substituents:
      5-Methoxy, F, $(CH_3)_2N$
      5-Methoxy-6-F, 2-Methyl
   b. Benzoyl substituents:
      P- Cl, F or CH_3S
   c. Acetic acid substituents:
      α-CH_3, CO_2CH_3
2. The carboxyl group is necessary for anti inflammatory activity. The more acidic the carboxyl group, the greater the antirheumatic activity.
3. The 1-indene isostere has activity similar to that of indomethacin.

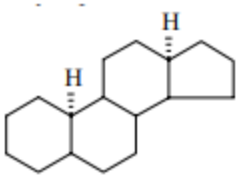
Steroids:

Saturated derivatives of phenanthrene and Ring D is Cyclopentane ring.

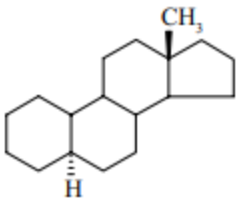
Basic Moiety in Steroids



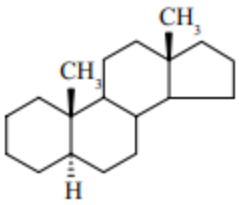
Cyclopentano perhydro phenanthrene



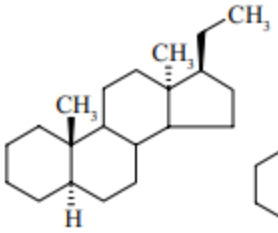
Gonane (C = 17)



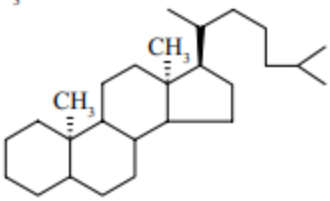
5 .-Estrane (C = 18)



5 . -Androstane (C = 19)



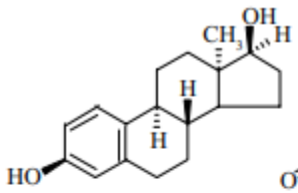
5 . -Pregnane (C = 21)



Cholastane (C=27)

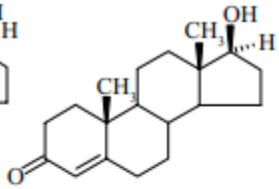
- Meaning of α- Behind the plane
- Meaning of β- Above the plane

Nomenclature of steroids:



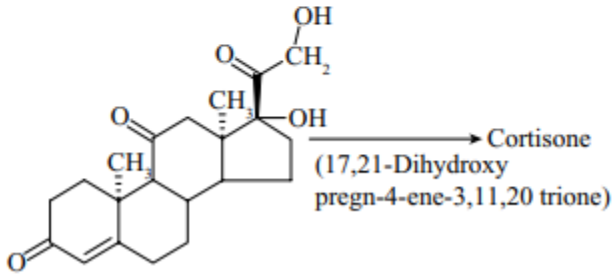
17 -Estradiol

(Estra-1, 3, 5 (10)-triene-3, 17 **β** diol)



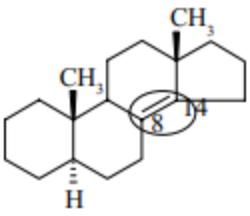
Testasterone

(17 **β**-Hydroxy androst-4-ene-3one)



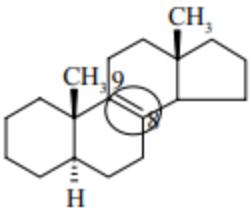
Cortisone

(17,21-Dihydroxy pregn-4-ene-3,11,20 trione)



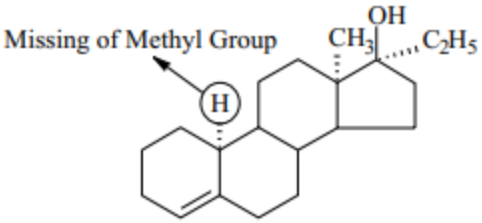
5 .-Androst-8(14)-ene

(Double bond is not In sequence)



5 .-Androst-8-ene

(When double bond is in sequence, we only mention the number at d.b starts)



17 .-ethyl-19-norandrost-4-en-17 -ol

When methyl group is missing from basic moiety, then we have to write nor at which number of carbon is the methyl group removed.

Stereochemistry:

In 5 α- steroids A/B rings are in trans form

In 5 β- steroids A/B rings are in Cis form

Chain form is more stable than boat form due to less angle strain and hence all cyclohexane rings in the steroid nucleus exists in the chair conformation.

Cholestane , androstane and pregnane can be exists into two conformations i.e, chair form and boat form.

Classification of steroids:

Anti-inflammatory agents: e.g: Cortisone

Sex hormones: e.g: estrogen, Progesterone and testosterone

Oral contraceptives: e.g: Nor-ethisterone

Cardiac steroids: e.g: Digitoxigenin

Diuretics: e.g: Spiranolactone

Antibiotics: e.g: Fusidic acid

Neuromuscular blockers: eg: Pancuronium bromide

Vitamin D precursor: e.g: Ergosterol

Sex Hormone:

1. Hormone activity is controlled by GnRH hormones like FSH, LH/ICSH and Luteoprin/Prolactin

2. LHRh agonist-Nafarelin

Classification:

a. **Human oestrogens and derivatives:** These are naturally occurring oestrogens in humans
   e.g: Estrone, Ethinyl estradiol and estriol

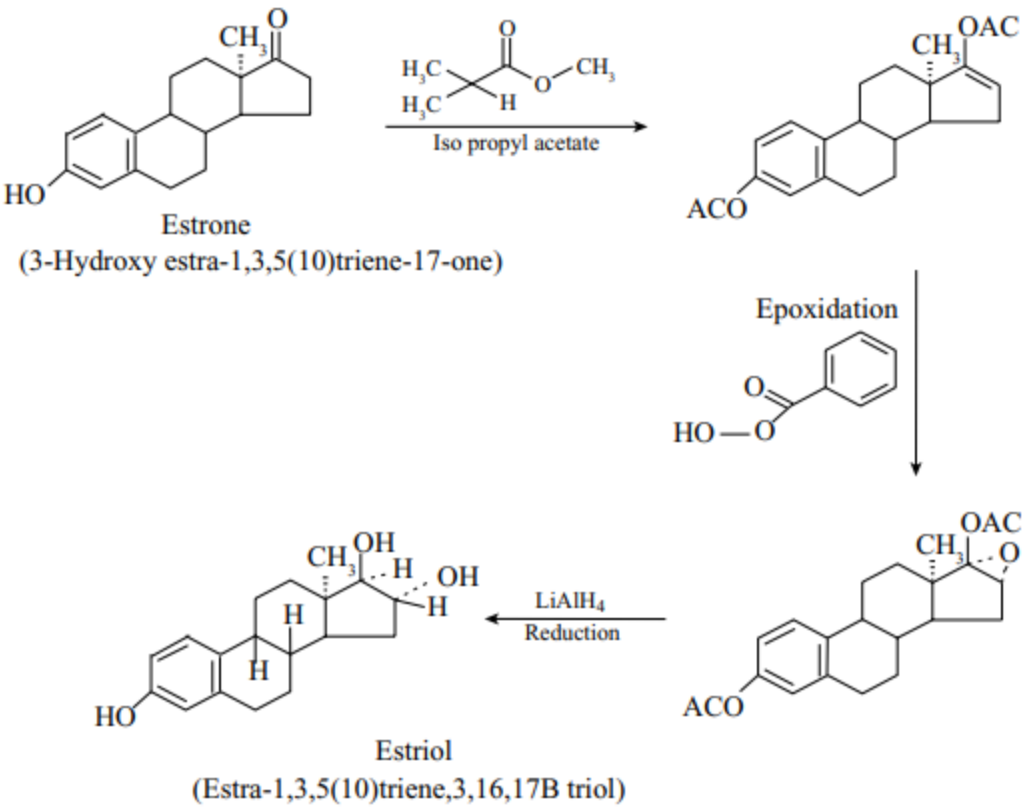
b. **Stallion oestrogens:** stallion excretes more estrogen than any other living form.

   e.g: equillin, Equilenin

c. **synthetic or non-steroidal oestrogens:**

   e.g: Diethylstilbestrol, Chlorotrianisene, dienestreol, Benzestrol

Synthesis of estroil:



Estrone
(3-Hydroxy estra-1,3,5(10)triene-17-one)

Estriol
(Estra-1,3,5(10)triene,3,16,17B triol)

Androgens and anabolic agents:

Androgenic activity: It includes normal development, functioning and maintainance of the male sex organs and sexual characteristics. Androgens are formed from C-21 steroids.

Anabolic activity: It causes nitrogen retention by increasing the protein synthesis, decreasing the rate of protein catabolism and thus promotes laying down of new tissues.

Eg: Testosterone

Structural activity relationship:

1. A steroidal skeleton is minimum structural requirement to have androgenic activity.
2. Testosterone is not effective orally, because metabolic occur at 17-β oxygen which is important to attachment to the receptor site.
3. 5 α-androstane has androgenic activity, Ring expansion, ring contraction and change in configuration at C-5 leads to reduce or destroy the androgenic and anabolic activity.
4. Introduction of an sp^2 hybridized carbon atom into the ring A renders the ring more planar results greater anabolic activity.

Drugs acting on CNS:

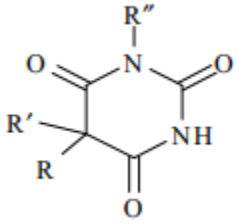
General anaesthetics: General anaesthetic is a class of CNS depressant drugs which produce partial or total loss of the sense of pain with a controlled and reversible depression of the functional activity of CNS.

Classification:

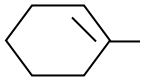
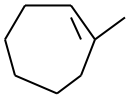
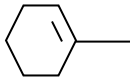
1. Hydrocarbon: e.g: Cyclopropane, Ethylene
2. Halogenated Hydrocarbons: e.g: Halothane, Ethyl chloride
3. Ether: e.g: Diethyl ether, vinyl ether
4. Alcohol: e.g: Trichloroethanol
5. Ultra short acting barbiturate: e.g: Thiopental sodium, Methohexital sodium
6. Miscellaneous agents: e.g: Nitrous oxide, Ketamine HCl, Propanidid

Sedatives and Hypnotics:

1. **Barbiturate** :
   General structure:



Name	R	R’	R”
1. Long acting Barbiturates:			
Barbital	H	C_2H_5	C_2H_5
Phenobarbital	H	C_2H_5	C_6H_5
Mephobarbital	CH_3	C_2H_5	C_6H_5

2. Intermediate acting Barbiturates:			
Amobarbital	H	C_2H_5	$CH_2CH_2CH(CH_3)_2$
Butabarbital	H	C_2H_5	$CH\text{-}CH_2CH_3$ | CH_3
3. Short acting barbiturates:			
Cyclobarbital	H	C_2H_5	
Heptabarbital	H	C_2H_5	
4. Ultra short acting barbiturates:			
Hexobarbitone	CH_3	CH_3	
Thiopentone	H	C_2H_5	$CH\text{-}CH_2CH_2CH_3$ | CH_3

Structural activity relationship:

1,3,5,5- tetra substituted barbituric acid are inactive since they are not acidic. They upon metabolism, produce 1,5,5- trisubstituted barbituric acids, which are acidic.

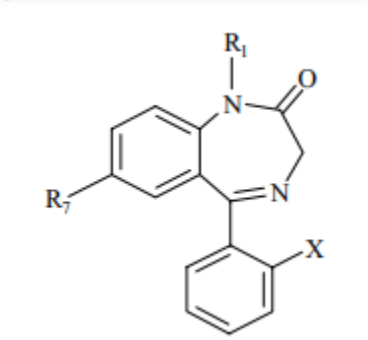
The sum of the carbon atoms of both substituents at carbon 5 should bebetween 6 and 10 inorder to attain optimal hynoptic activity.

Alicyclic or aromatic substituted analogues are more potent than analogues with aliphatic substituents with the same number of carbon atoms.

Introduction of a halogen atom into the 5-alkyl substituent increases potency.

Benzodiazepine:

General structure:



Name	R_1	R_7	X
Oxazepam	H	Cl	H
Nitrazepam	H	NO_2	H
Quazepam	CH_2CF_3	Cl	Cl
Lorazepam	H	Cl	H
Temazepam	CH_3	Cl	H

Structural activity relationship:

1. All CNS- depressant benzodiazepine are usually substituted with a 5- aryl or 5-cyclo-hexenyl group.
2. Position 7, if substituted with electron withdrawing groups, results into an enhancement of activity, while substitution elsewhere in this aromatic ring results in decreases in activity.
3. It is an anti-anxiety benzodiazepine related compound completely devoid of anti-convulsant and sedative properities.

Ureides derivative: Example: Apronalide, Bromasuvalum, Capuride, Cabromal. All are bromine containing compounds are very toxic because of bromism.

Piperidinedione derivative: Example : Methgyprylon, Glutethimide.

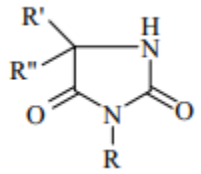
Chloral derivative: Chlorobutanol, Dichlorophenazone.

Carbamate derivative: Meprobamate which is central muscle relaxant and anti-anxiety.

Amide derivative: Triacetamide, Valuoctamide, Oxonamide

ANTI CONVULSANTS:

A. Hydantoins:
General structure:



Name	R	R'	R"
Phenytoin	H	C_6H_5	C_6H_5
Mephenytoin	CH_3	C_2H_5	C_6H_5
Ethotoin	C_2H_5	H	C_6H_5
Phenylethylhydantoin	H	C_6H_5	C_2H_5

Structure-Activity Relationship:

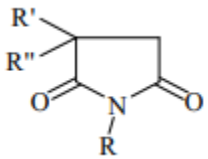
A 5- Phenyl or other aromatic substituent is essential for he activity.

Alkyl substituents at position 5 may contribute to sedation, a property absent in phenytoin.

Among other hydantoins, like spirohydantoins, thiohydantoins, dithiohydantoins and 1,3-disubstituted hydantoins, some exhibit activity against chemically induced convulsions while remain ineffective against electroshock induced convulsions.

Succinimide derivative:

General structure:



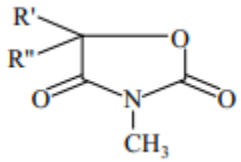
Name	R	R’	R”
Phensuximide	CH_3	H	C_6H_5
Methsuximide	CH_3	CH_3	C_6H_5
Ethosuximide	H	CH_3	C_2H_5

Structure Activity Relationship:

1. Methsuximide and Phensuximide have phenyl substituents which make them active against electrically induced convulsions.
2. N-methylation decreases activity against electroshock seizures and impart more activity against chemically induced convulsions.
3. α- MethylalkoxyPhenyl succinimides and alkoxybenzylsuccinimides were active anticonvulsant. The length of the alkoxy group here determines the activity.

Oxazolidinediones:

General structure:



Name	R’	R”
Trimethadione	CH_3	CH_3
Paramethadione	CH_3	C_2H_5

Structure Activity relationship:

The nature of the substituents on C_5 is important e.g: lower alkyl substituents tendsto anti petitmal activity while aryl substituents towards anti grandma activity

The N-alkyl substituent does not affect the activity and undergo N-dealkylation I metabolism E.g; The anticonvulsant activity of trimethadione is due mainly to its N-demethylated metabolite, dimethadione.

Aliphatic Carboxylic acid derivative:

E.g: Valproic acid

Sodium valproate

Phenyltriazine derivative:

e.g: Lamotrigine

Benzodiazepine derivative:

e.g: Clonazepam

Diazepam

Clobazepam

Drugs acting on CVS:

Anti-Arrhythmic agents:

Classification:

Class I:Local Anaesthetics:

Class IA: Membrane – depressant drugs:

Eg: Quinidine, Procainamide, Diisopyramide

IB: Short period:

Eg: Lidocaine, Phenytoin, Mexilitin, Tocainide

IC: Flecainide, Encainide, Lorcainide

II. β- adrenergic drugs:

E.g: Alprenolol, Atenolol, Metoprolol, Practolol, Propanolol, Pindolol

III .Amoidarone, Bretylium, D-sotalol

IV.Selective Ca^{++} antagonist:

E.g: Nifedepine, Verapamil, Diltiazem

Class V Miscellaneous agents:

E.g: Atropine, Neostigmin, Edrophonium

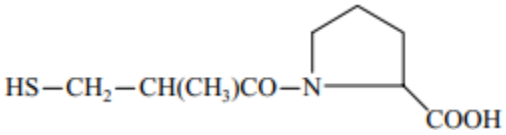
Antihypertensive Drugs:

Drug acting on Renin angiotensin system:

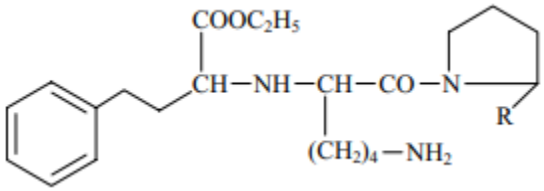
(1) Renin inhibitor
Ex: Propanolol, Clonidine, Enalkiren, Ramikiren, Terlakiren, Zankiren, Diltiazem.

(2) ACE inhibitor
Mechanism of action:
i. It inhibits conversion of angiotensin–I to angiotensin-II
ii. It also increases bradykinin level and vasodialation

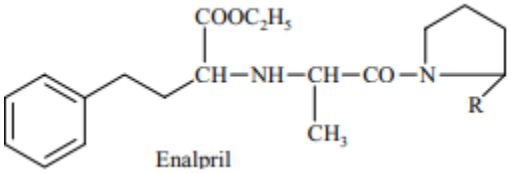
Ex: Captopril



Lisinopril



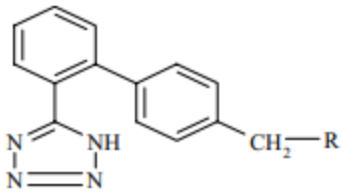
Enalpril

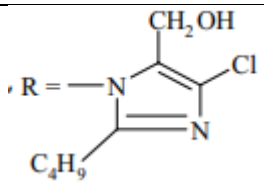
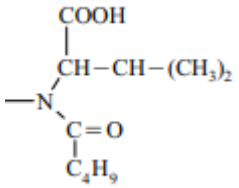


Enalpril

(3) Angiotensin-II antagonist with AT1 receptor blocker:

General structure:



Name	R	characteristic
Losartan		It contains imidazole ring
Valsartan		It is valine containing ring
Candesartan	It contains benzimidazole with ester group	-

Anti Anginal drugs:

Angina pectoris: When imbalance between oxygen supply and oxygen demand in myocardium occurs this is called as angina pectoris.

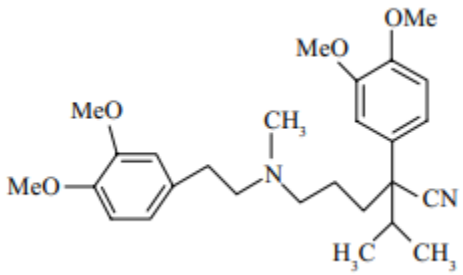
Classification of Anti Anginal agents:

1. Nitrate derivative:
   (a) short acting drugs:
   Amyl nitrate/isopentyl nitrate: Currently used in cyanide poisoning treatment.
   Glyceryl trinitrate (nitroglycerin): It is given sublingually and duration of action is 30 min.
   Isosorbide nitrate: It is a bicyclic form of sorbitol.
   • It is given sublingually or as chewable tablet.
   • Specific side-effect: Tachycardia
   Erythrityl tetranitrate:
   Pentaerythritol tetranitrate: It is a powerful explosive and must be diluted with lactose or mannitol.

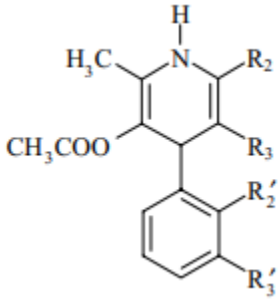
Calcium channel blocker:

1. Phenyl alkyl amine derivative:

(a) First generation agent: Verapamil



2. 1, 4 dihydropyridine derivatives:
   General structure:



Name	R_2	R_3	R_2’	R_3’
Nifedepine	CH_3	$COOCH_3$	NO_2	H
Amlodipine	CH_2-O-C_2H_4-NH_2	$COOC_2H_5$	Cl	H
Felodipine	CH_3	$COOC_2H_5$	Cl	Cl
Nimodipine	CH_3	COO-C_2H_4-OCH_3	H	NO_2
Nitrendipine	CH_3	$COOC_2H_5$	H	NO_2

Newer third generation drugs:

E.g:Lacidipine

Monatepil

Potassium channel blockers:

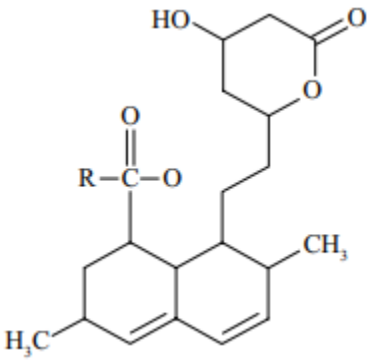
Nicorandil, Pinacidil and Cromakalim are potassium channel opener and bronchodialator which are used in angina as well as in asthma.

Anti Hyperlipidemics:

These antihyperlipidemic drugs are specifically used in artherosclerosis.

HMG-CO-A reductase inhibitors:

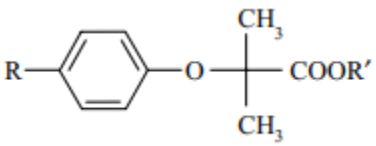
General Structure:



SNO.	Name	R
1.	Lovastatin	$CH(CH_3)$– CH_2 –CH_3
2.	Simvastatin	$C(CH_3)_2$ –C_5H_{11}

Fibric Acid derivative:

General structure:



Name of the drug	R	R’
Clofibrate	Cl	C_2H_5
Fenofibrate	$Cl{-}C_6H_5$-C=O	$CH{-}(CH_3)_2$
Ciprofibrate	$CH\text{-}Cl_2$	H

Bile acid binding resin:

1) Cholestyramine: It is styrene copolymer of divinyl benzene and quaternary ammonium compound.
2) Colestipol: High mol.wt granular copolymer of tetraethyl pentamine and epichlorohydrin.
3) Cosevelam: Recent drug which does not cause constipation.

ANTI DIABETIC AGENT:

Type of diabetes:

(1) Type-1 dibetes (IDDM)/juvenile onset:
Insulin deficiency occurs due to destruction of β cell.
(2) Type-2 diabetes (NDDM)/Maturity onset.
Insulin resistance occurs.

Classification:

Short acting agent:

SNO.	Insulin Preparation
1.	Regular insulin
2.	Amorphous insulin zinc suspension (Semilente)
3.	Insulin aspart
4.	Insulin lispro

Intermediate acting:

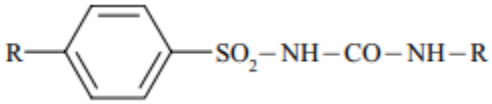
SNO.	Insulin preparation
1.	Globin zinc insulin
2.	Lente suspension
3.	NPH (Neutral protamine hagedorn)

Long acting:

SNO.	Insulin Preparation
1.	Protamine zinc insulin
2.	Ultralente
3.	Glarbine Insulin

Type II Diabetes mellitus:

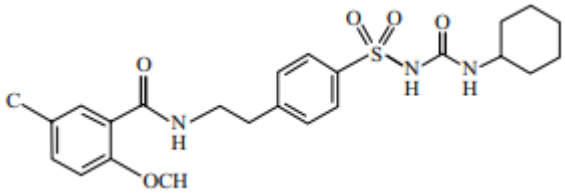
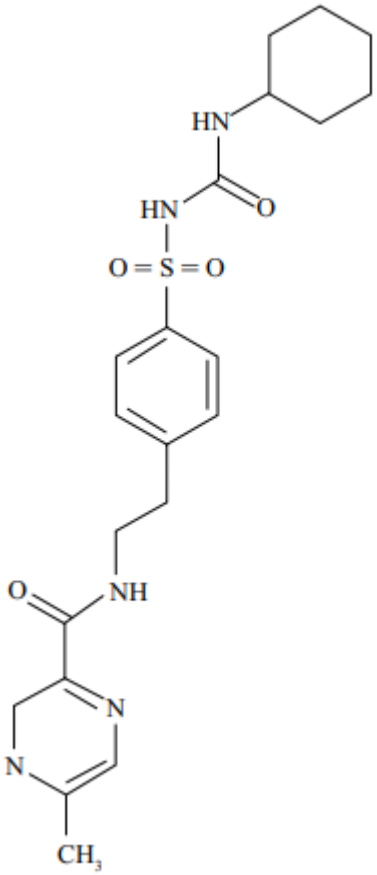
1. Sulfonyl derivative:
   General structure:

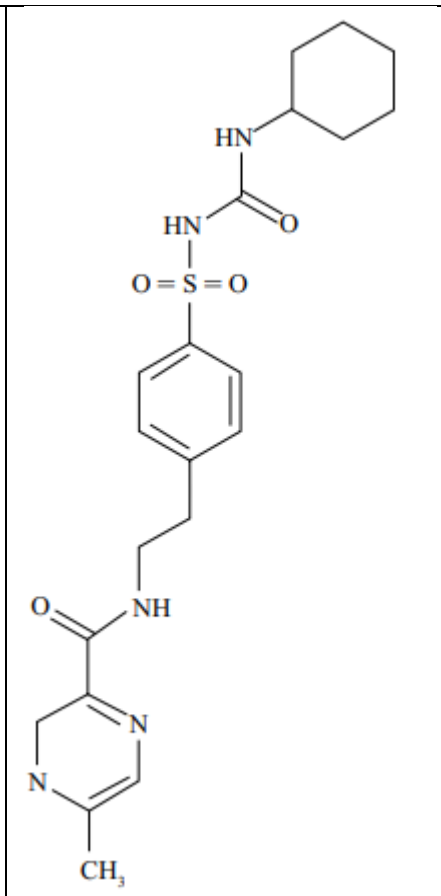


First generation durgs:

Name	R	R’
Tolbutamide	CH_3	C_4H_9
Chloropropamide	Cl	C_3H_7
Acetohexamide	CH_3CO	Cyclohexane ring
Tolazamide	CH_3	Azepine ring

Second generation drugs:

Name	Structure
Glibenclaimide	
Glipizide	



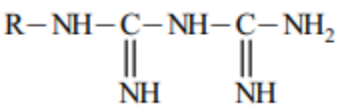
Non sulfonyl urea derivatives:

Repaglinide

Nateglinide

Biguanide derivative:

General structure:



1) Phenformin: R = $-C_6H_5-CH_2-CH_2$

2) Metformin: R = $(CH_3)_2-N-$

(D) Alpha glucosidase inhibitors:

e.g: Acarbose, Miglitol, Varcabose

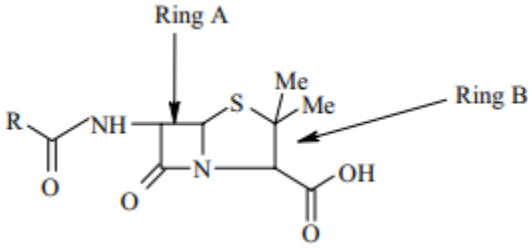
(E) Thiazolidinediones derivative:

e.g: Rosiglitazone, Pioglitazone

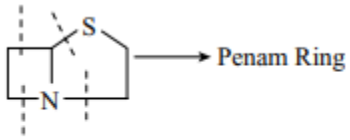
ANTIBIOTICS:

Classification:

1. β-lactum antibiotics:
   General structure:



All penicillin has penam ring as a basic moiety.



1-Aza-4-thia-Bicyclo [3.2.0] heptane

Eg: Ampicillin, Amoxicillin, Carbenicillin, Oxacillin, Cloxacillin

Structural activity relationship:

1. All β-lactum antibiotics contain a 4 membered β-lactum ring which is fused through the nitrogen and tetrahedral carbon atoms to a second hetero cyclic ring.
2. Penicillins consist of β-lactum ring fused with thiazolidine.
3. Thienamycins consist of β-lactum ring with pyrrolline ring.
4. Clavulanic acid consist of β-lactum fused with oxazolidine ring
5. Cephalosporins consist of β-lactum fused with a six membered dihydrothiazine ring.

Synthesis of ampicillin:

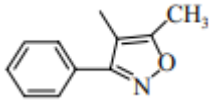
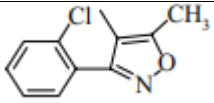
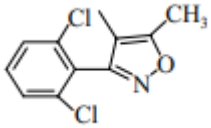
i. $C_6H_5CHO + NH_4Cl + NaCN \longrightarrow C_6H_5\underset{\displaystyle CN}{\underset{|}{C}}H\text{-}\ NH_2 + NaCl + H_2O$

ii. $C_6H_5CH(CN)\text{-}NH_2 + 2HCl + H_2O \longrightarrow C_6H_5CH(NH_2)\text{-}COOH + NH_4Cl$

iii. $C_6H_5CH(NH_2)\text{-}COOH \longrightarrow C_6H_5CH(NH_2)\text{-}COCl$

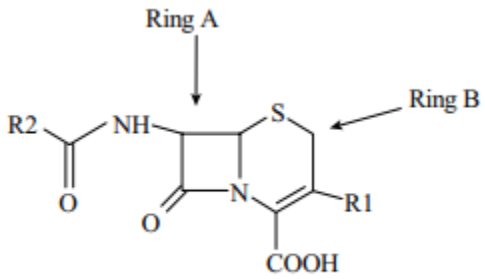
Phenyl Glycine

iv. $C_6H_5CH(NH_2)\text{-}COCl$ + 6-APA/ Acetone $\longrightarrow$ Ampicillin

Name	R
Oxacillin	
Cloxacillin	
Dicloxacillin	

Cephalosporin:

General structure:



First generation drugs:

Cephaloridine, Cephalothin, Cephapirin, Cephalexin, Cephaloglycine, Cefadroxil, Cephadrin, Cefazolin

Second generation drugs:

Cefamandole, Cefoxitin, Cefuroxime, Cefaclor

Third generation drugs:

Ceftizoxime, Cefotaxime, Ceftazidime, Ceftriaxone, Cefmenoxime, Moxalactum

Structural activity relationship:

1. The semi synthetic cephalosporins are obtained by attaching a side-chains of 7-amino cephalosporinic acid just as pencillins are made from 6- aminopenicillanic acid.
2. Cephalosporins are significantly less sensitive than β-lactamase resistant penicillin to hydrolysis by the enzymes from staphylococcus aureus and Bacillus subtilis.
3. Phenylglycine moiety if attached to 7-amino cephalosporanic acid, affords a compound with increased oral activity.
4. A sulfonic acid moiety if present in acyl side-chain, confers antipseudomonal activity to certain penicillins.
5. While screening for β- lactum antibiotic stable to β-lactamases, a strain of streptomyces lactamdurans was found to release certain agents containing 6-α-methoxy group whose electronic and steric properities protect the antibiotic from enzymatic attack.

Macrolide antibiotic:

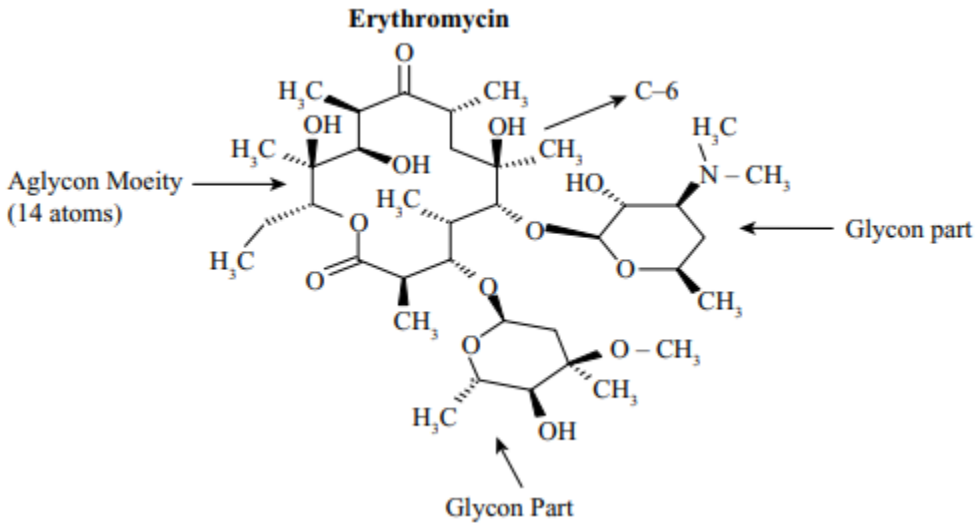
Sources: Actinomycetes

Picromycin is the first identified drug in macrolide antibiotic.

E.g., Spiramycin, Oleanlomycin, Erythromycin

Semi-synthetic derivative of erythromycin:

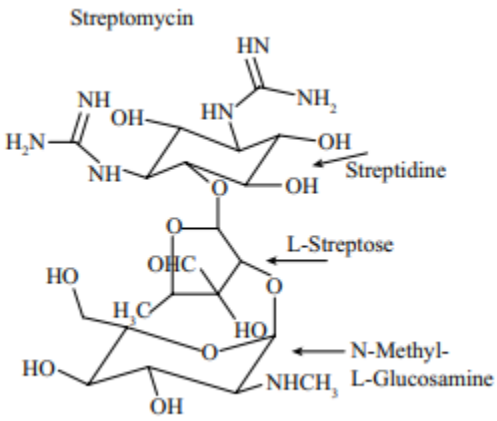
Roxithromycin , Dirithromycin, Clarithromycin, Azithromycin



Aminoglycoside Antibiotics:

- Chemically, it is aminosugar obtained from actinomyces.
- A highly substituted 1,3-diaminocyclohexane central ring is present in the form of deoxystreptamine in all members except streptomycin and dihydro streptomycin.

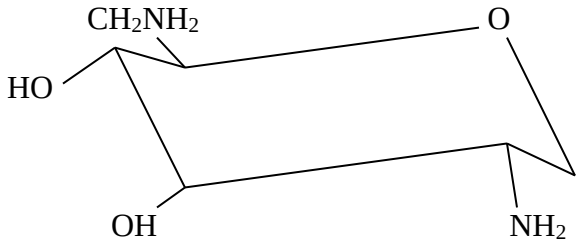
Aminoglycosides	Obtained from
Streptomcin	Streptomyces griseus
Kanamycin	Streptomyces kanamyceticus
Tobramycin	Streptomyces tenebrarius
Gentamycin	Micromonospora purpurea
Neomycin	Streptomyces fradiae



SAR of aminoglycosides:

1. The amino group at C-6 and C-2 serve as major target sites for bacterial inactivating enzymes.

2. Clevage of 3-hydroxy or the 4-hydroxyl or both groups does not affect the activity.



3. The acylation and ethylation though not increases the activity, helps to retain the anti bacterial potency.

4. In Sisomycin series, 2-hydroxylation and 5-deoxygenation results in increased inhibition of bacterial inactivating enyme systems.

Tetracycline:

1.Carbon atom 4, 4a, 5, 5a, 6 and 12a are potentially chiral

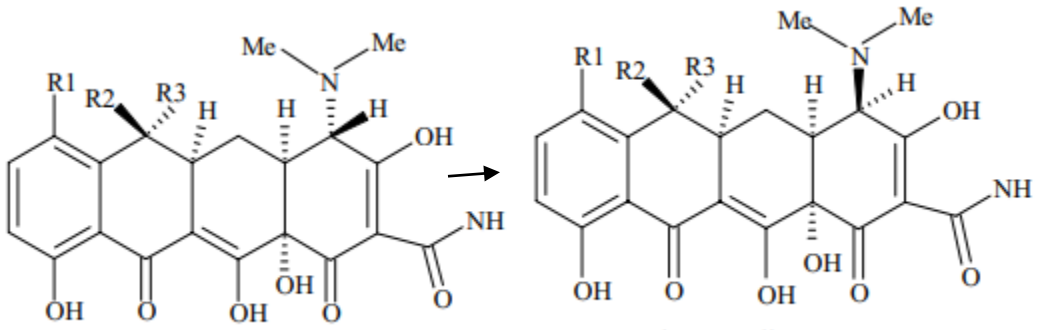
2. Oxytetracycline and doxycycline each with 5α-OH substituents have six asymmetric centres while others have only five asymmetric centres

3. The basic ring present in Tetracycline is polycyclic napthacene carboxamide.

4. All Tetracycline are amphoteric in nature

5. At pH-7, it is converted into Zwitterion.

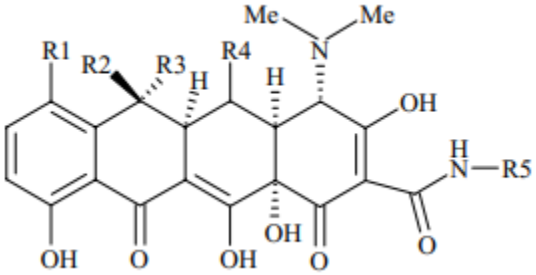
6. Ability to undergo epimerization at C-4 in solution of neutral pH range (7)



Tetracyclin Epi tetracyclin

SAR of Tetracycline:

General structure :



1. Tetracyclines are the broad spectrum antibiotics and the basic nucleus common to all tetracyclines is a polycyclic napthacene carboxamide which is comprised of fused, six membered rings A, B, C and D. This backbone skeleton is essential for activity.
2. The enolized system present at carbons 1 to 3 must be intact for good activity.
3. Epitrtacyclines are very much less active than neutral isomers.
4. A cis type fusion between A/B wuth an α-hydroxyl group at 12ais necessary for retention of activity.
5. The clinically effective mannich bases are rolitetracycline,lymecycline, and clomocycline.

Name	R_1	R_2	R_3	R_4	R_5	
7-chlortetracycline	Cl	CH_3	OH	H	H	
Oxytetracycline	H	CH_3	OH	OH	H	
Tetracycline	H	CH_3	OH	H	H	

Demeclocycline	Cl	H	OH	H	H	
Methacycline	H		$=CH_2$	OH	H	
Doxycycline	H	CH_3	H	OH	H	
Minocycline	$N(CH_3)_2$	H	H	H	H	
Lymecycline	H	CH_3	OH	H	Y	

Anti-Tuberculosis Agent:

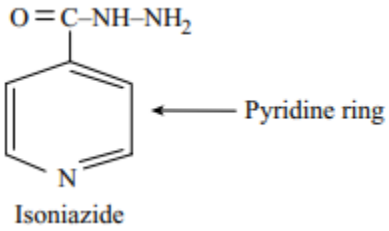
Tuberculosis: It is a disease of respiratory transmission. A person gets infected when he comes in contact with the environment contaminated with viable tuberculi bacilli. It spreads through coughing, sneezing and shouting of infected person.

Classification:

First line agents:

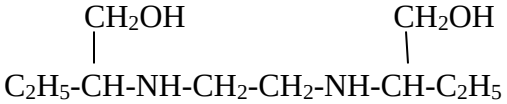
- Streptomycin
- Isoniazid
- Ethambutol
- Rifampin

Structure of Isoniazid:



Isoniazide

Structure of Ethambutol:

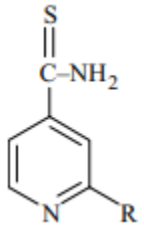


Second line agents:

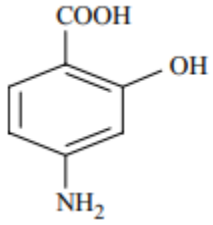
- Ethionamide
- p-Aminosalicylic caid

- Pyrazinamide
- Thiacetazone
- Cycloserine
- Capreomycin and vlomycin

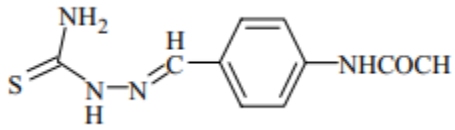
Structure of Ethionamide:



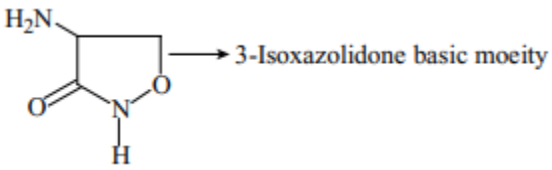
Structure of p-Amino salicylic acid:



Structure of Thiacetazone:



Structure of Cycloserine:



Structural activity relationship:

1. It may interfere in peptide synthesis by acting as antimetabolite and inhibiting the incorporation of sulfur (-SH) containing amino acid. (Cysteine, methionine)
2. Because of sour taste and irritant nature, this drug is mainly used in form of its Na+ , K+ and Ca+ salts.
3. Thiacetazone is thiosemicarbazone derivative.

4. Cycloserin is a analogue of D-alanin and chemically D-4-amino3-isoxazolidone.
5. Capreomycin is more potent and less toxic than viomycin
6. Nephrotoxicity, skin rashes and ototoxicity are major side effects.

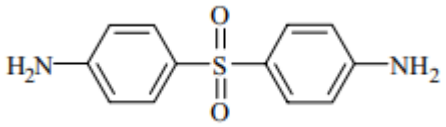
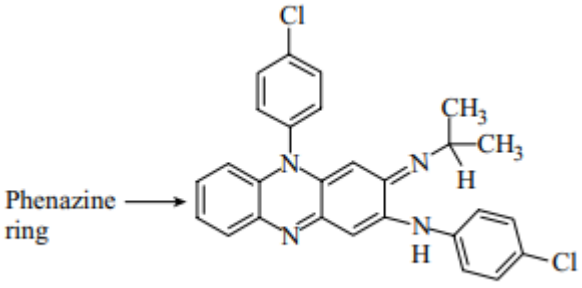
Anti Leprotic Agent:

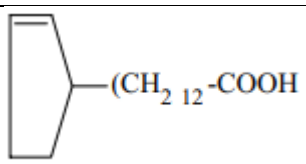
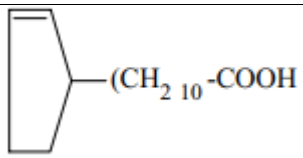
Leprosy is a chronic disease caused due to acid fast bacilli which produce nodules in the skin and loss of sensation in affected region.

Lepra reaction-It is hypersensitivity reaction not occuring as a result of allergy to drug but they should considered as allergic reaction to metabolite product of infected microorganism.

Types of leprosy:

1. Tuberculoid Leprosy: Presence of infection in restricted area. Dapson treatment is required
2. Lepromatous Leprosy: Infection is spread in wide area of body, so multi-drug treatment is required.
3. Indeterminate Leprosy: It is the early stage of disease, m.o are not multiplied to the extent to induce lepra reaction
4. Borderline leprosy: Tuberculoid leprosy and Lepromatous leprosy are two extreme forms of the disease. All forms that lie in between these two forms is known as borderline leprosy.

Name	Structure
Dapsone	
Clofazimine	

Chaulmogric acid	
Hydnocarpic acid	

QSAR- Methods:

1. The introduction of Hansch method in 1964 enabled chemists to describe SAR-Studies in quantative terms.
2. QSAR started to develop from a merely intuitive and empirical discipline to more and more advanced state.
3. Various methods used in QSAR analysis can be
    - Free energy models
    - Other statistical methods
    - Pattern recognition
    - Topological methods
    - Quantum Mechanical Methods
    - Molecular modeling

ORGANIC CHEMISTRY

ATOMIC STRUCTURE:

An atom consists of negatively charged electrons, positively charged protons, and neutral neutrons

Atomic number: numbers of protons in its nucleus (E.g., ^{6} C, ^{7} N, ^{8} O)

Mass number: the sum of number of protons and neutrons in a atom (E.g., $^{12}_{6}$ C, $^{14}_{7}$ N)

Characteristics of protons, neutrons and electrons:

	Protons	Electrons	Neutrons
Charge	Unit positive	Unit Negative	Charge less
Mass	Nearly as the same of that mass of the H_2 atom	$1/1837^{th}$ the mass of proton or H_2 atom	Very close to the mass of H_2 atom
Symbol	$^{1}_{+1}P$ $^{1}_{+1}H$	$^{1}_{-1}e$	$^{1}_{0}n$

Isotopes have the same atomic number but different mass numbers (E.g., $^{12}_{6}$ C, $^{13}_{6}$ C, $^{14}_{6}$ C)

Isobars are atoms of different elements having the same atomic mass but different atomic number.

Isotopes are chemically same and physically different. But the converse is true in isobars. That is, isobars are elements which are chemically different but physically same. Since their number of electrons is different, their chemical properties are different. Examples of isobars are Fe^{58} and Ni^{58}.

Isotones

Isotones are elements having the same number of neutrons. Examples of isotones are Chlorine-37 and Potassium-39. Both have 20 neutrons in their nuclei

The atomic weight: The average weighted mass of its atoms

Molecular weight: The sum of the atomic weights of all the atoms in the molecule.

Distribution of electron in an atom				
	First shell	Second shell	Third shell	Fourth shell
Atomic orbitals	s	s p	s p d	s p d f
No. of atomic orbitals	1	1,3	1,3,5	1,3,5,7
Maximum no. of electrons	2	8	18	32

Electronic configuration of some smallest elements:

Atoms	Atomic no	1S	2S	2Px	2Py	2Pz	3S

H	1	↑					
He	2	↑↓					
Li	3	↑↓	↑				
Be	4	↑↓	↑↓				
B	5	↑↓	↑↓	↑			
C	6	↑↓	↑↓	↑	↑		
N	7	↑↓	↑↓	↑	↑	↑	
O	8	↑↓	↑↓	↑↓	↑	↑	
F	9	↑↓	↑↓	↑↓	↑↓	↑	
Ne	10	↑↓	↑↓	↑↓	↑↓	↑↓	
Na	11	↑↓	↑↓	↑↓	↑↓	↑↓	↑

Hybridization:

The process of mixing and recasting to form same number of equivalent orbitals with maximum symmetry and definite orientation in space is called hybridization.

concept of hybridization:

To explain valencies of element.

To explain equivalence of bonds.

To explain geometry of molecule.

Types of Hybridization:

Sp3 -Hybridization: Mixing and recasting of's' orbitals with three 'p' orbital of same atom forming four identical orbitals tetrahedrally arranged in space.

Sp2 -Hybridization: One's' and two 'p' orbitals of the same atom mix and form three identical orbitals trigonally arranged in space.

Sp-Hybridization: One's' and one 'p' orbital of the same atom mix and form two identical orbitals diagonally arranged in space.

Hybridization involving d-orbitals:

Some 3rd row and larger elements can accommodate more than eight electrons around the central atom. These atoms will also be hybridized and have very specific arrangements of the attached groups in space. The two types of hybridization involved with d orbitals are sp3 d and sp3 d2

The groups will be arranged in a trigonal bipyramidal arrangement with sp3 d hybridization...bond angles will be Chapter 243.32 120^{o} in the plane with two groups arranged vertically above and below this plane.

Sigma Bonds:

This particular kind of covalent bond in which electrons are shared between atoms is called a sigma bond.

The sigma-bond is defined as the linear overlap of atomic orbitals (hybrids except for hydrogen) in which two electrons are directly between the two bonded nuclei.

The distinguishing feature of a sigma bond (or sigma bonding orbital) is that the overlap region lies directly between the two nuclei.

Linear overlap along inter-nuclear axis

Bond is rotationally symmetrical along inter-nuclear axis and Stronger than Pi-bond.

Pi Bonds:

Pi bonds involve the electrons in the leftover p orbital (unhybridized) for each carbon atom. Those p orbitals are the electron clouds or orbitals that are shown going up above and below each carbon atom

Pi-bonds are defined as the parallel overlap of p-orbitals. A double bond has one sigma-bond and one pi-bond. A triple bond thus consists of a sigma-bond and two pi-bonds with the pi-bonds in different planes.

The overlapping occurs in two places, above and below the sigma bond. The pi bond does not overlap in the region directly between the two carbon atoms where the sigma bond is formed.

It is Lateral overlap perpendicular to inter-nuclear axis.

It is not rotationally symmetrical and weaker than sigma bond.

Bond dissociation energy:

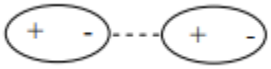
The amount energy is consumed or liberated when a bond is formed or broken is called bond dissociation energy.

Intramolecular forces: within the molecules is known as intramolecular force.

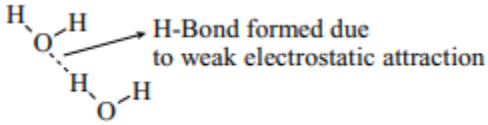
- Repulsive forces
- Attractive forces

Intermolecular forces: between two molecules is known as inter molecular force

- **Dipole – dipole interaction:**



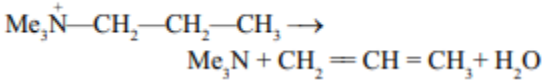
- **Hydrogen bonding:** H atom serves as a bridge between two most electro negative atom is known as H-bonding.
  Intermolecular H-bonding:



  Intramolecular H-bonding: Eg: Salicylic acid
- **Vanderwaal forces:** Related to non polar solvents.

Hofmann Rule:

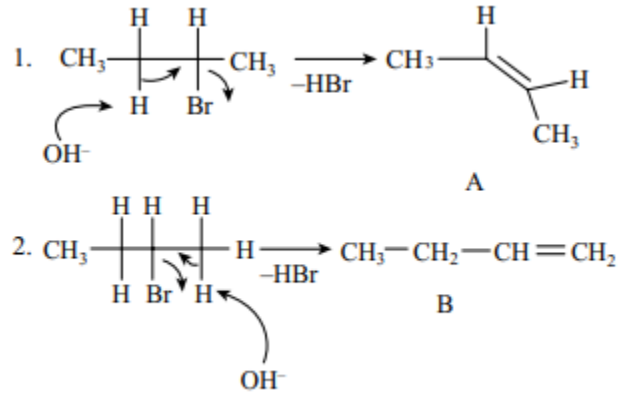
When 4° ammonium hydroxide is strongly heated (≤125°C) it decomposes to yield a 3° amine, water and alkene is known as β-elimination.



It states that in case of alternative β-hydrogen in the charged substrate (4° ammonium); the least substituted alkene is predominantly formed.

Saytzeff Rule:

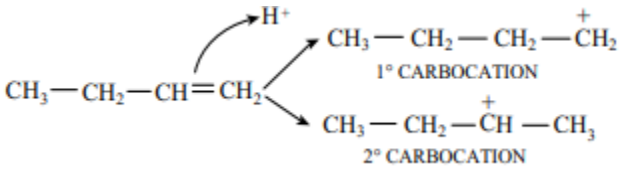
De-hydro halogenation of secondary-and tertiary-alkyl halides proceeds by the preferential removal of the hydrogen from the carbon that has the smallest number of hydrogens.



According to Saytzeff's rule, a is more substituted alkene which is more stable and easily formed.

Markonikov's Rule:

When an acidic reagent is added to –C=C-than the positive portion of reagent goes to the side of double bond or triple bond contain more H.



According to the rule, 2° carbocation can easily formed compared to 1° carbocation.

Stereochemistry:

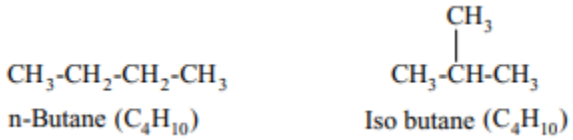
Stereochemistry is the study of the three dimensional shape of molecules and the effects of shape upon the properties of molecules.

Isomers are compounds that have the same molecular formulas but different structural arrangements of atoms.

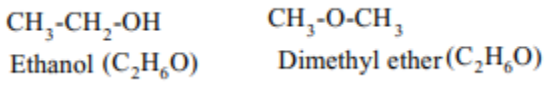
- **Constitutional isomer:** Constitutional isomers include butane and isobutane (both have the molecular formula C4 H10, but different structures and ethanol and dimethyl ether (both have the formula C2 H6 O, but again the two differ structurally.
- **Stereo isomer:** Stereo isomers are isomers whose constituent atoms are connected in the same sequence, but in different spatial patterns.

Structural isomers:

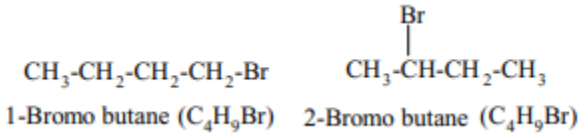
1. **Chain isomers:** Structures having a similar molecular formula but differ in arrangement of carbon chain are known as chain isomer.



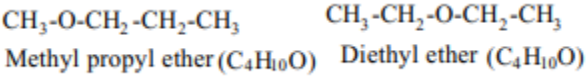
2. **Functional isomers:**Structures having a similar molecular formula but differ in functional group are known as functional isomer.



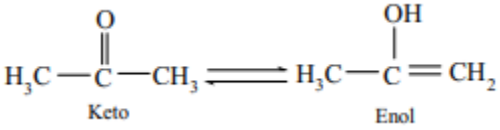
3. **Positional isomers:** Structures having a similar molecular formula but differ in position of functional group are known as positional isomers.



4. **Metamerism:** Unequal distribution of carbon chain on either side of functional group is known as Metamerism.



5. **Tautomerism:** The existence of two or more chemical compounds that are capable of facile interconversion is known as Tautomerism.

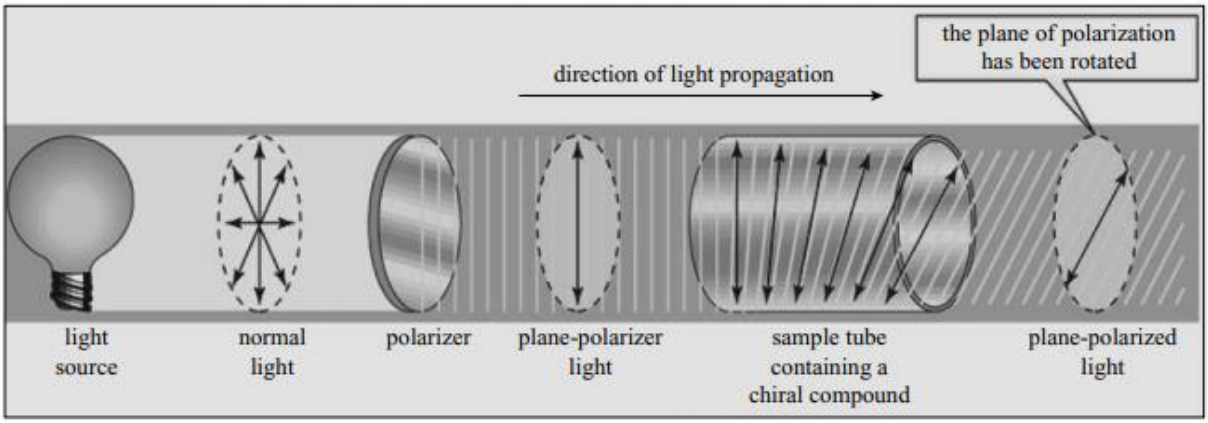


Optical isomer (d and l):

Optically active compound: A compound which rotates the plane polarized light is known as optically active compound.

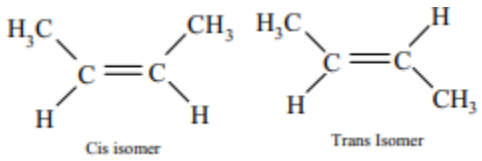
- Chiral compounds are optically active; they rotate the plane of polarized light.
- Achiral compounds do not rotate the plane of polarized light. They are optically inactive.
- If the compound rotates the plane polarized light to the right side, then it known as Dextrorotatory compound. [d or (+)].

- If the compound rotates the plane polarized light to left side, then it known as laevorotatory compound. [l or (–)].



Racemic mixture, which contains an equal amount (equi-molar mixture) of the two enantiomers, is optically inactive.

Cis-Trans system:

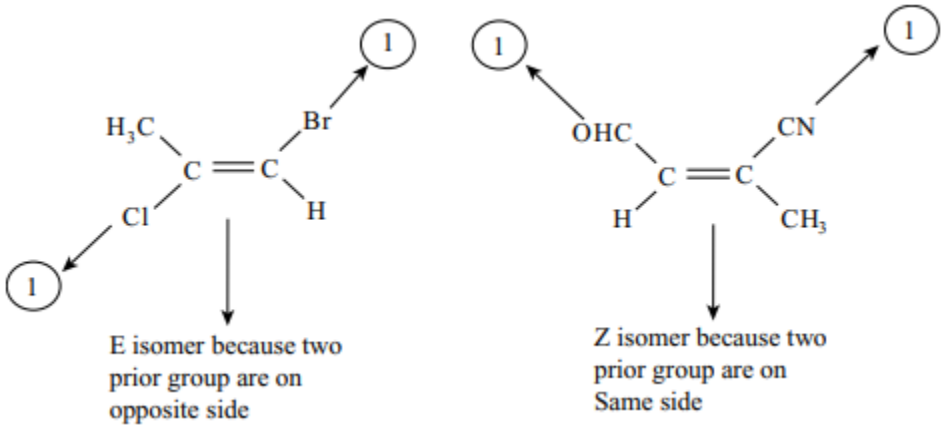


- Cis means two similar groups are on same side.
- Trans means two similar groups are on opposite direction.
- Trans isomer is more stable than Cis isomer due to steric hindrance is more with cis isomer because two bulky groups are in same side.

E/Z system: In alkenes, if carbon is attached with four different groups than it will be nomenclatured by E/Z system.

E means Entegegen-Opposite side

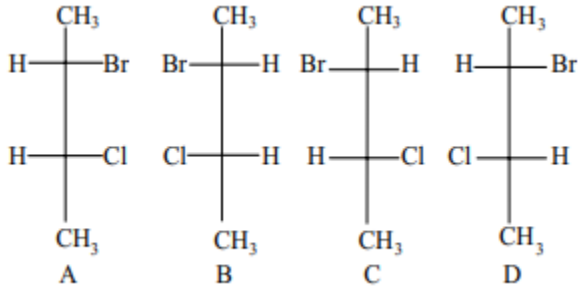
Z means Zusammen-Same side



Enantiomer and Diastereomer:

Enantiomer: The stereoisomer of compounds which are non-superimposable mirror image of each other are known as enantiomers.

- Enantiomers are often referred as a optical isomer
- Chirality is necessary and sufficient condition for existence of an enantiomer.
- It is also a necessary but not sufficient condition for optical activity.
- E.g., Racemic mixture is optically inactive.
- All enantiomer have similar physical property (exception is specific rotation) while different chemical property.



- A and B and C and D are pair of enantiomer
- While A and C, A and D, B and C and B and D are pair of diastereomer.

Stereoselectivity:

Any chemical reaction that yields predominantly, one stereoisomer, out of several stereoisomer possibilities is said to be a stereoselective reaction.

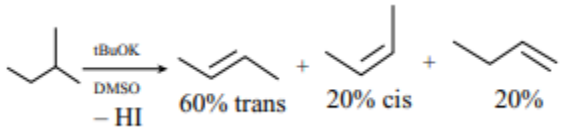
An enantioselective reaction is the one in which one enantiomer is formed in preference to the other, in a reaction that creates an optically active product from an achiral starting material, using either a chiral catalyst, an enzyme or a chiral reagent. The degree of selectivity is measured by the enantiomeric excess. An important variant is kinetic resolution, in which a pre-existing chiral center undergoes reaction with a chiral catalyst, an enzyme or a chiral reagent such that one

enantiomer reacts faster than the other and leaves behind the less reactive enantiomer, or in which a pre-existing chiral center influences the reactivity of a reaction center elsewhere in the same molecule.

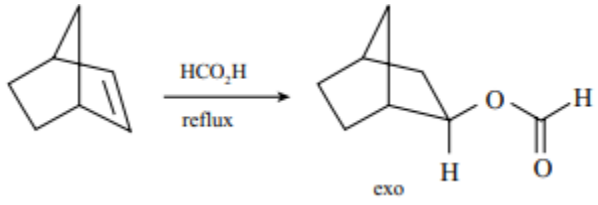
A diastereoselective reaction is the one in which one diastereomer is formed in preference to another (or in which a subset of all possible diastereomers dominates the product mixture), establishing a preferred relative stereochemistry. In this case, either two or more chiral centers are formed at once such that one relative stereochemistry is favoured, or a pre-existing chiral center (which needs not be optically pure) biases the stereochemical outcome during the creation of another. The degree of relative selectivity is measured by the diastereomeric excess.

Stereoconvergence can be considered an opposite of stereoselectivity, when the reaction of two different stereoisomers yields a single product stereoisomer.

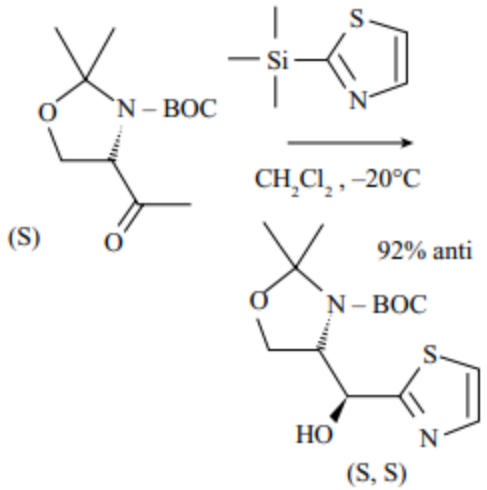
An example of modest stereoselectivity is the dehydrohalogenation of 2-iodo-butane which yields 60% trans-2-butene and 20% cis-2-butene. Since alkene geometric isomers are also classified as diastereomers, this reaction would also be called diastereoselective.



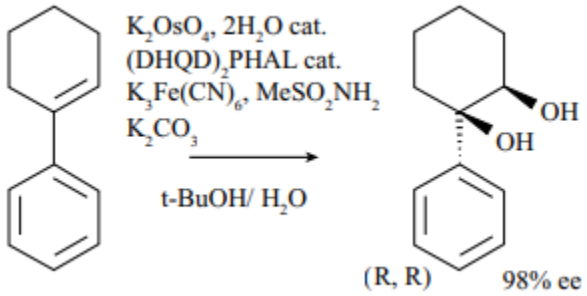
The addition of formic acid to norbornene is also stereospecific because the exo isomer is formed exclusively without any of the endo isomer.



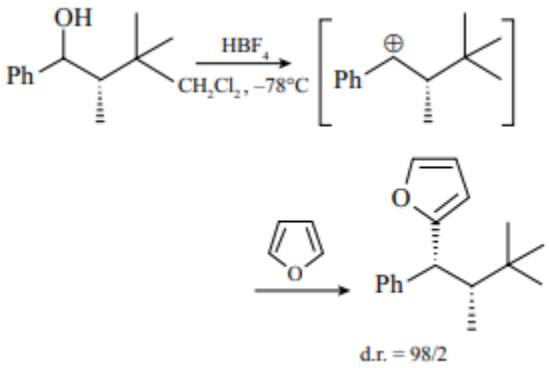
Cram's rule predicts the major diastereomer resulting from the diastereoselective nucleophilic addition to a carbonyl group next to a chiral center. The chiral center need not be optically pure, as the relative stereochemistry will be the same for both enantiomers. In the example below, the (S)-aldehyde reacts with a thiazole to form the (S, S) diastereomer but only a small amount of the (S, R) diastereomer.



The sharpless epoxidation is an example of an enantioselective process, in which an achiral allylic alcohol substrate is transformed into an optically active epoxyalcohol. In the case of chiral allylic alcohols, kinetic resolution results. Another example is sharpless asymmetric dihydroxylation. In the example below, the achiral alkene yields only one of possible four stereoisomers



With a stereogenic center next to the carbocation, the substitution can be stereoselective in intra and intermolecular reactions. In the reaction depicted below, the nucleophile (furan) can approach the carbocation formed from the least shielded side away from the bulky t-butyl group resulting in high facial diastereoselectivity

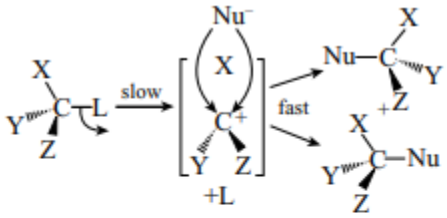


Stereospecificity:

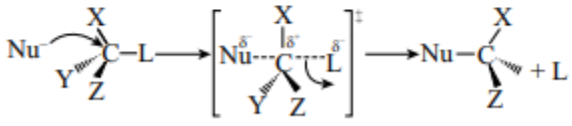
Stereospecificity is the property of a reaction mechanism that leads to different stereoisomeric reaction products from different stereoisomeric reactants, or which operates on only one (or a subset) of the stereoisomers.

A stereospecific mechanism specifies the stereochemical outcome of a given reactant, whereas a stereoselective reaction selects products from those made available by the same, non-specific mechanism acting on a given reactant. Given a single, stereoisomerically pure starting material, a stereospecific mechanism will give 100% of a particular stereoisomer (or no reaction), although loss of stereochemical integrity can easily occur through competing mechanisms with different stereochemical outcomes. A stereoselective process will normally give multiple products even if only one mechanism is operating on an isomerically pure starting material.

Stereospecificity in substitution reactions:



S_N1 mechanism non-stereospecific

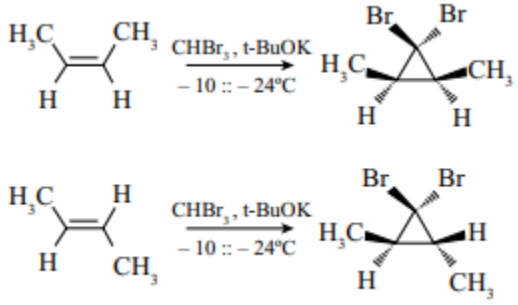


S_N2 mechanism stereospecific

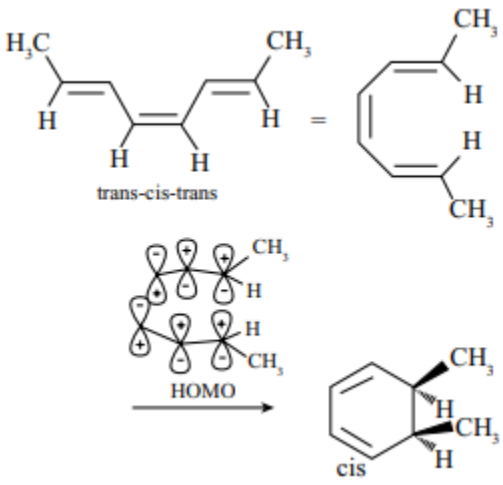
Tertiary centres react almost exclusively by the SN1 mechanism whereas primary centres (except neopentyl centres) react almost exclusively by the SN2 mechanism. When a nucleophilic substitution results in incomplete inversion, it is because of a competition between the two

mechanisms, which often occurs at secondary centres, or because of double inversion (as when iodide is the nucleophile).

The addition of carbenes to alkenes is stereospecific in that the geometry of the alkene is preserved in the product. For example, dibromocarbene and cis-2-butene yield cis-2, 3-dimethyl-1, 1-dibromocyclopropane, whereas the trans isomer exclusively yields the trans cyclopropane.



The disrotatory ring closing reaction of conjugated trienes is stereospecific in that isomeric reactants will give isomeric products. For example, trans, cis, trans-2, 4, 6-octatriene gives cis-dimethylcyclohexadiene, whereas the trans, cis, cis reactant isomer gives the trans product and the trans, trans, trans reactant isomer does not react in this manner.



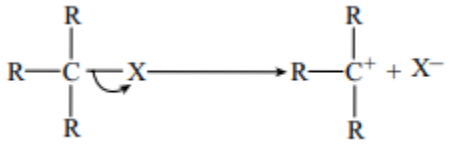
1. **SN1 mechanism:**

   SN1 indicates a substitution, nucleophilic, unimolecular reaction,

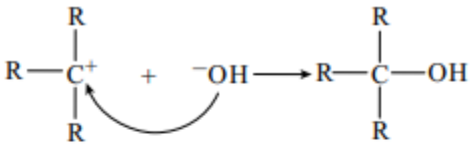
   Rate = k[R–X] follows first order kinetics

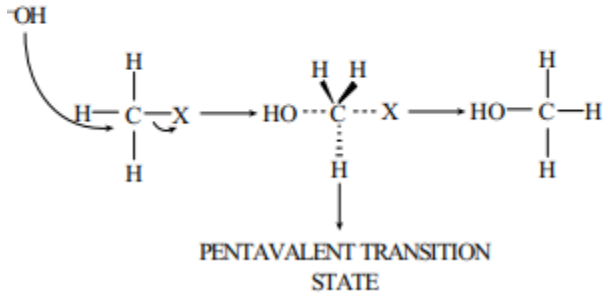
   This implies that the rate determining step of the mechanism depends on the decomposition of a single molecular species.

Step-1 Generation of carbocation, slow step, rate determining step.:



Step-2 Rapid attack of nucleophile on carbocationic carbon.





Reactivity order 3° >2°>1° alkyl halides

2. **SN2 mechanism:**

SN2 indicates a substitution, nucleophilic, bimolecular reaction, described by the expression

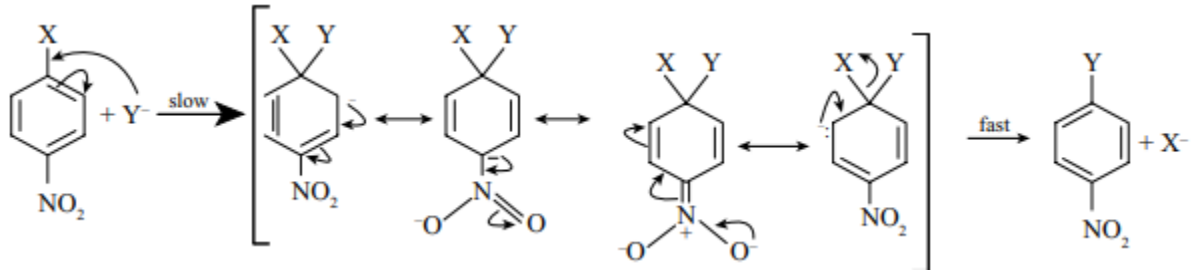
Rate = k [Nu][R–X]. It follows second order kinetics.

Reactivity order 1˚ >2˚ >3˚ alkyl halides

Halides Nucleophilicity in protic solvents: F < Cl < Br < I, because nucleophile is solvated.

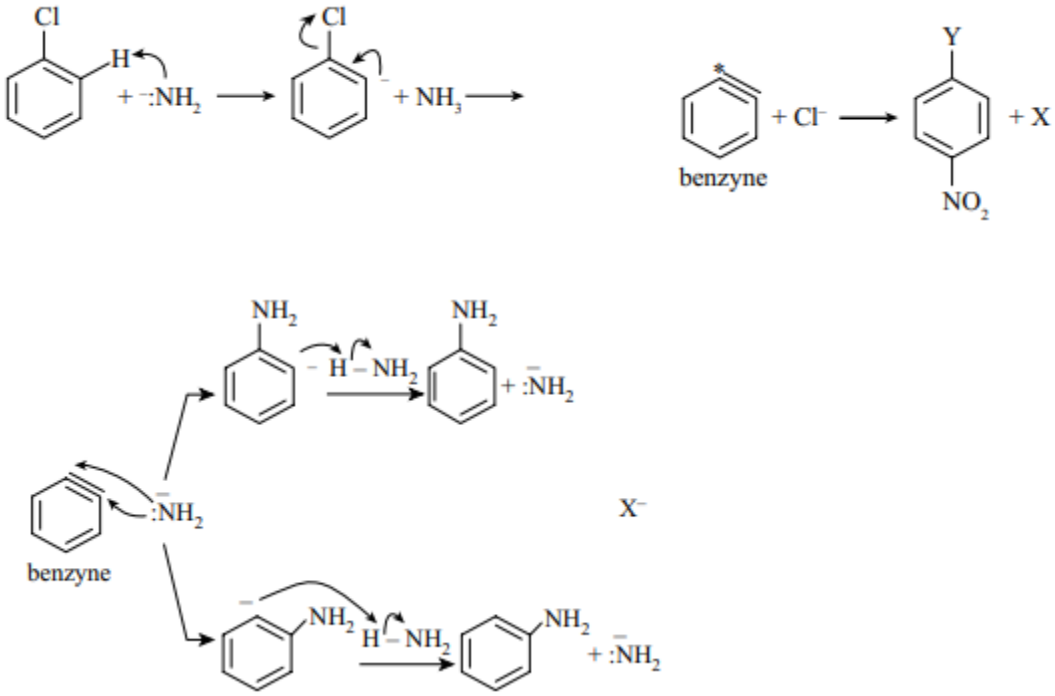
Halides Nucleophilicity in Aprotic solvents: F > Cl > Br > I, because nucleophile is not solvated.

General mechanism for nucleophilic aromatic substitution:



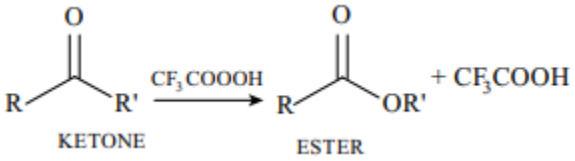
Benzyne mechanism or aryne mechanism or benzyne mechanism:

It requires strong basic condition.

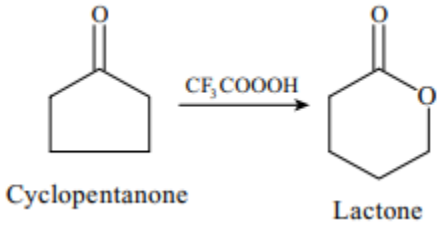


Rearrangements:

1. **Baeyer-villiger rearrangements:**
   - Baeyer-Villiger rearrangements is an example of the migration of a group from carbon to electron deficient oxygen.
   - The reaction involves oxidation of ketones to esters by treatment with paracids such as per benzoic acid, pertrifluoroacetic acid etc.

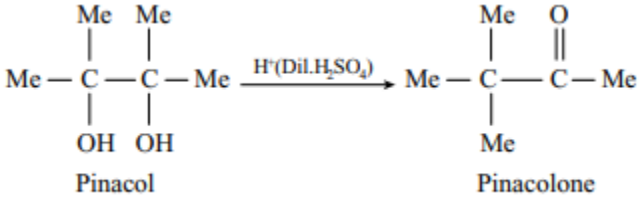


   - Cyclic ketone is converted into the lactone with ring expansion

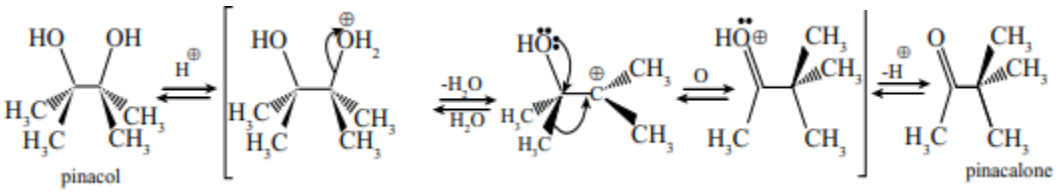


2. Pinacole-pinacolone rearrangements:

The acid catalysed rearrangements of vic. diols (1, 2-diols) to ketone or aldehyde with elimination of water is known as pinacol-pinacolone rearrangement.



Mechanism of pinacole-pinacolone rearrangements:

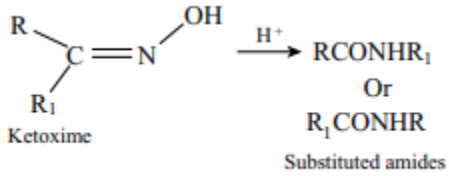


3. Beckmann rearrangement:

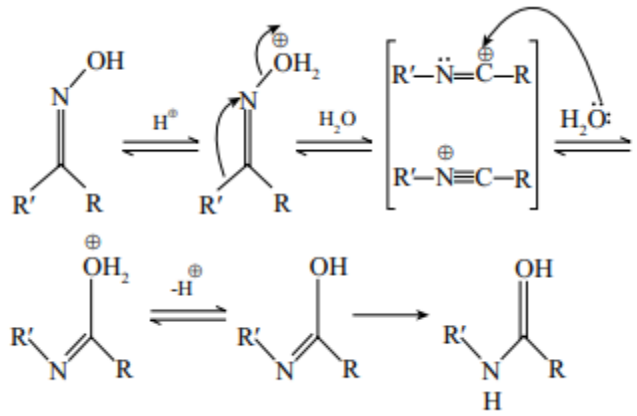
The acid catalysed conversion of ketoxime to N-substituted amides is known as Beckmann rearrangement.

The reaction is catalysed by acidic reagents such as H_2SO_4 , $SOCl_2$, P_2O_5 , PCl_5 , C_6H_5 , SO_2Cl.

The reaction involves migration of group from carbon to nitrogen.

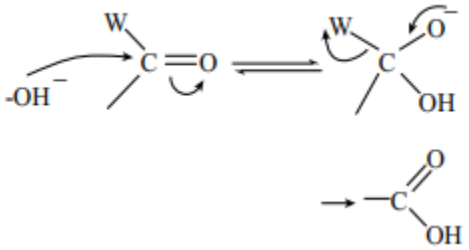


Mechanism of beckmann rearrangement:

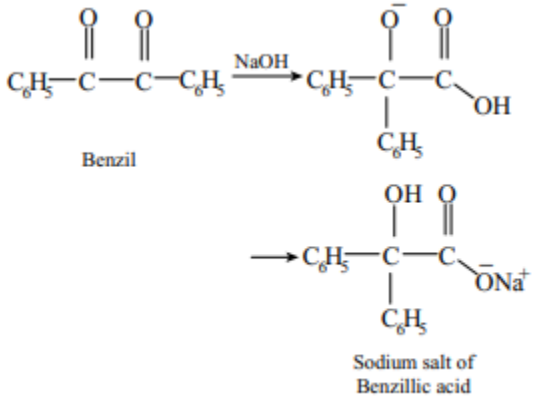


4. Benzillic acid rearrangement:

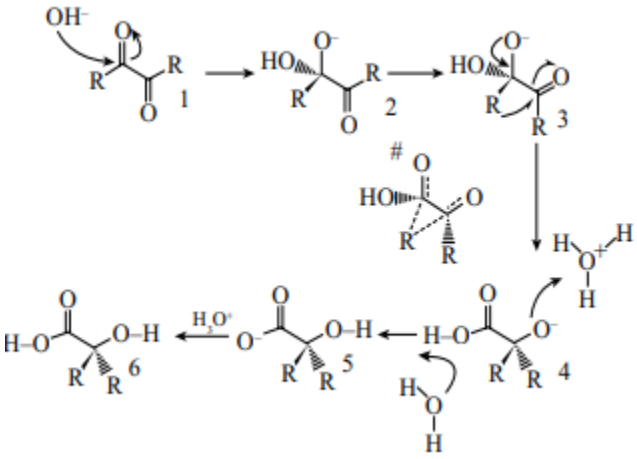
The addition of a strong base to a carbonyl group results in the formation of an anion. The reversal of the anionic charge may cause removing of attached group W.



In 1, 2-diketone the group W may migrate to the adjacent electron-deficient carbonyl carbon, forming -hydroxy acid.



Mechanism of benzillic acid rearrangement:



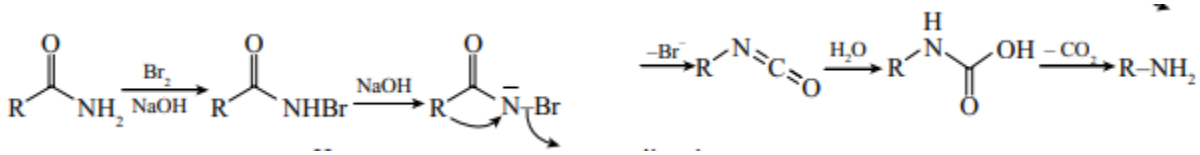
5. Hofmann rearrangement or Hofmann bromamide reaction:

The reaction involves the conversion of an amide to a primary amine (1°) with one carbon less, by the action of alkaline hypohalite (NaOH solution + Br_2 or Cl_2)

$$RCONH_2 + Br_2 + {}_4NaOH \rightarrow RNH_2 + {}_2NaBr + Na_2CO + {}_2H_2O$$

Bromine is mostly used in this reaction and the intermediate is N-bromamide.

Mechanism of Hofmann rearrangement:



PHARMACOLOGY

General Anaesthetics

Classification:

I. **Inhalational Geranal Anaesthetics:**
   - **a)** Volatile liquids: Chloroform, diethyl ether, ehtyl chloride, enlurance, Halothane, Isoflurane
   - **b)** Gases: Cycloprapane, Nitrous oxide

II. **Non volatile General Anaesthetics**
   - **a) Ultra Short Acting Barbiturates:** Thiopental, Methohexital
   - **b) Non Barbiturates:**
     - i. Pencyclidine derivative: Ketamine
     - ii. Steroid: Althesin, Pregnanedione
     - iii. Etomidate, Profol

Neuroleptanalgesia: Neuroleptics are a group of drugs which induce a state of apathy & mental detachment in which the patient is mildly sedated & uncaring about his surroundings. Neuroleptalgesia is a method of IV anaesthesia which comines the use o neuroleptic drug with a opioid analgesic drug which relieves pain. Ex: *Droperidol, Fentanyl, Alentanil, Remifentanil.*

Drugs commonly used or Preanaesthetic medication are:

a) Morphine, Pethidine, Buprenorphine
b) Sedative & tranquilizers: Diazepam, Nitrazepam
c) Anticholinergic drugs: Atropine/Scopalamine
d) Antiemetics: Promethazine, Trimeprazine.

SEDATIVES-HYPNOTICS

Classification:

I. Urea derivatives:
   a) Diureides: Barbiturates
   b) Related Ureids: Glutethimide, Methyprylone
II. Benzodiazepines
III. Alcohols: Chloral hydrate
IV. Aldehydes: Paraldehyde
V. Acetylated carbinols: Ethinamate
VI. Imidazopyridine: Zolpidem

VII. Miscellaneous: Meprobamate, Methaqualone, scopolamine

Barbiturates: They facilitate inhibitory neurotransmission in the CNS by interacting with receptors adjacent to the GABA chloride ionophore complex to open chloride ion channels & hyperpolarize neuronal membrane.

Barbital Poisoning: Mannitol, Furosemide have been employed to increase urinary elimination of barbiturates.

Barbiturate classification:

a) Long Acting (> 8 hr): Phenobarbitone
b) Intermediate acting (4-8 hr): Amylobarbitone, Butobarbitone, Pentobarbitone
c) Short acting (< 4 hr): Secobarbitone, Hexobarbitone
d) Ultra Short Acting: Thiopentone, Kemithal, Methohexitone

Benzodiazepines: They act on GABA-A receptors surrounding the chloride ion channel in the CNS.

Chloral Hydrate: Small doses induce sedation, larger doses at bed time results in sleep.

Paraldehyde: It is given by rectal or IM route to induce hypnosis. It is also used as an anticonvulsant in status epilepticus, tetanus & eclampsia.

Sleep Walking & Nightmares Medicines : Diazepam, Flurazepam

EPILEPTIC DRUGS

The characteristic pathophysiologic event in a seizure is believed to be paroxysmal depolarization shit of neuronal membrane potential & associated burst discharge. Excitatory neurotransmitters, such as aspartate & glutamate are thought to e involved in the initiation & spread of the seizure discharge and inhibitory transmitter (GABA) is believed to be responsible for formation of seizure activity. The underlying neurochemical defect in epilepsy may be impairment in the inhibitory GABA mechanism.

Antiepileptic Drugs:

1. Hydantoin derivatives: Phenytoin, methotoin, ethotoin
2. Barbiturates: Phenobarbitone, Primidone, Mephobarbitone
3. Iminostilbenes: Carbamazepine

4. Succinimides: Ethosuximide, Methsuximide
5. GABA transaminase inhibitors: Sodium valproate, vigabatrin
6. GABA re-uptake inhibitors: Tiagabin
7. GABA agonists: Gabapentin
8. Benzodiazepines: Clonazepam, diazepam, Clobazam
9. Miscellaneous: Acetazolamide, Sulthiame, Amphetamine, Phenacetamide.

PHENYTOIN: It inhibits spread of seizure discharges in the brain & shortens the duration of after-discharge. The drug causes dose-dependent block of Sodium channels, thus reducing the neuronal sodium cone, leading to a reduction in post-tetanic potentiation & to increase neuronal potassium concentration.

Phenobarbitone acts like Phenytoin.

CARBAMAZEPINE: Used in treatment of temporal lobe & Grand mal seizures. Acts as phenytoin. Also useful in trigeminal neuralgia, diabetic neuropathy, cancer & multiple sclerosis, glossopharyngeal neuralgia.

ETHOSUXIMIDE: It is effective only in Petit Mal Epilepsy.

Sodium Valproate: It acts by inhibition of GABA transmission, potentiation of post-synaptic GABA activity & decreasing brain levels of excitatory amino acids.

Vigabatrin: Same as Sodium valproate.

Tiagabine: It is nipecotin acid analogue, which selectively increases the amount of inhibitory transmitter GABA of GABAergic synapses. It enhances GABAergic inhibition by decreasing neuronal & astrocytic re-uptake of GABA, leading to an increase in synaptic GABA.

GABAPENTIN: It is increases release of GABA.

CLONAZEPAM: It acts by increasing effectiveness of inhibitory neurotransmitter GABA within the CNS.

LAMOTRIGINE: It blocks influx of sodium ions, thereby inhibiting excitatory amino acid glutamate in the brain. It acts by blocking N-methyl D-aspartate (NMDA) receptors. It is used as add on treatment in patients with partial & secondarily generalized seizures that are resistant to other antiepileptic drugs.

SULTHIAME: Used in temporal lobe epilepsy.

ACETAZOLAMIDE: Used effectively in Petit Mal seizures.

OPIOID ANALGESICS

Opioid drugs produce their effects by combining with opioid receptors which are widely distributed in the CNS and other tissues. The opioid receptors have been classified into Mu, delta and kappa types.

Some peptides with strong opiate like analgesic & receptor binding activity are present in CNS & other tissues.

Betaendorphins: Derived from Pituitory gland. It is pain modulator in the CNS. Affinity to Mu receptors.

Enkephalins: They present in pituitary gland, brain, GI Tract, spinal cord, pancreas, adrenal cortex. Affinity to Delta receptors.

Betadynorphin: Widely distributed in CNS. Affinity to kappa receptors.

MORPHINE: Morphine raises pain threshold, thereby reducing the perception of pain. This action assisted by feeling of wellbeing. It is used in acute Myocardial infarction, fracture of long bones, acute pericarditis, spontaneous pneumothorax, in acute left ventricular failure, to reduce constipation.

CODEINE: It enhances analgesic effect of aspirin & combined with it. Used as antitussive.

PAPAVERINE: Used as a coronary dilator & in peripheral vascular disease.

NOSCAPINE: Used as antitussive.

HEROIN: More analgesic than morphine, produce greater euphoria and higher dependence liability. 1 mg of Methadone can substitute for 2 mg of heroin for withdrawl symptoms.

APOMORPHINE: Potent emetic, the emesis due to activation of dopaminergic receptors which in turn stimulate emetic centre located in the area of nucleus fascicule sediterri. This effect is blocked by neuroleptics like chlorpromazine but not by anti-histamine.

Synthetic Morphine Substitutes:

I. Pethidine & its congeners: Piminodine, Fentanyl, Diphenoxylate
II. Methadone & its congeners
III. Morphinan compounds & its congeners: Levorphanol, Butorphanol
IV. Benzomorphan derivatives: Pentazocine
V. Miscellaneous: Nalbuphine, Buprenorphine

Pethidine used as an analgesic, Diphenoxylate used in treatment of diarrhoea, Loperamide is used for its selective constipative action.

Methadone used as an anaglesic & produce marked antitussive property. Levorphanol is more potent analgesic than morphine, is better absorbed on oral administration & produec less constipation.

Pentazocine has potent analgesic & weak opioid antagonist activity. Nalbuphine is both agonist & antagonist properties. As an agonist 3-4 times more potent than pentazocine while its antagonist property is about 10 times more potent than pentazocine.

Buprenorphine has both agonist & antagonist property.

Opioid Antagonists:

I. Pure antagonists: Naloxone
II. Partial agonists of Nalorphine: Nalorphine, Lavalorphan, cyclazocine
III. Partial agonists of Morphine type: Propiran, Profadol

Naloxone is selectively antagonizes respiratory depression action of morphine & other opioids. 1 mg o Naloxone completely blocks effects of 25 mg of heroin. Nalorphine used in treatment of acute morphine poisoning.

Cyclazocine is used for acute morphine intoxication & morphine addiction. Naltrexone is long acting, pure opioid antagonist.

NSAID

Hypothalamous plays important role in thermo-regulatory response. Two mechanisms control body temperature a) cutaneous vasodilatation b) increase sweat activity by sympathetic cholinergic fibres.

Lipopolysaccharadies of bacteria activate phagocytes to release IL1, TNF. TNF then act on vascular endothelial cells in hypothalamus & stimulate local synthesis of prostaglandins by hypothalamic cells. This causes fever.

Classification:

I. Salicylates & their congeners: Aspirin, salicylamide, Diflunisal, Sodium salicylate
II. P-aminophenol derivatives: Phenacetin, Paracetamol, Acetanilide
III. Pyrazolone derivatives: Phenylbutazone

IV. Indole derivatives: Indomethacin, Sulindac
V. Heterocyclic arylacetic acid derivatives: Diclofenac, Tolmetin, Ketorolac, Aceclofenac
VI. Propionic acid derivatives: Ibuproen, Fenoprofen, Naproxen, Ketoprofen
VII. Fenamates: Flufenamic acid, Mefenamic acid
VIII. Oxicams: Piroxicam
IX. Sulfonamides: Nimesulide
X. Miscellaneous: Nabumetone

Mechanism of Action: During inflammation, arachidonic acid is liberated from phospholipid fraction of cell membrane. It converted to prostaglandins through cyclooxygenase (COX-1, COX 2). COX 1 present in stomach, kidneys, blood vessels while COX 2 is inducible in activated leucocytes & other inflammatory cells. PGs sensitize blood vessels to the effects of mediators such as Bradykinins, 5-HT & Histamine that increase permeability. PGE, PGI produce hyperalgesia associated with inflammation.

Aspirin have both PG inhibition action & inhibition of T-lymphocyte activation and of their ability to release lymphokinases. Dicloenac & Indomethacin inhibit lipooxygenase pathway, thus decreasing production of leukotriens by leucocytes & synovial cells.

Salicylates: Salicylic acid, methyl salicylates are irritants, Salicylic acid also has keratolytic, antiseptic and fungistatic action. Useful or relieving pain of muscles & joints, dysmenorrhoea, toothache. Salicylates produce dyspepsia, peptic ulcer with gastrointestinal hemorrhage. For this salicylates given with Misoprostol (PGI analogues).

Aspirin inhibits platelet aggregation, it inhibits Adenosine diphosphate release from platelets. Further, by inhibiting COX, it suppresses Thomboxane A (TxA2) synthesis, in platelets.

Paracetamol has antipyretic, analgesic but poor anti-inflammatory action. Adverse effects are liver damage, hemolysis, skin reactions, neutropenia.

Phenylbutazone is potent anti-inflammatory drug. Used in gout, ankylosing sponhdylitis, Rheumatoid Arthritis & osteoarthritis.

CNS STIMULANTS

Classification:

a) **Acting directly on CNS**
   i)Predmominantly cortical stimulants: *Amphetamine, xanthine alkaloids, methylphenidate, pipradol*

ii)Predominantly medullary stimulants: *Picrotoxin*, *Pentylenetetrazol, amiphenazole, camphor, CO2, Nikethamide*

iii)Predominantly spinal stimulants: *Strychnine*

b) **Stimulate CNS relexly:** *Lobeline, Ammonia, Veratrum, Nicotine*

Xanthine alkaloids: Ex Caffeine, Theophylline, Theobromine. Threshold doses of caffeine act on cerebral cortex, larger amounts stimulate medullary centres & toxic doses result in convulsions as a result of entire neuraxis including spinal cord. Xanthine produce peripheral vasodilatation. They produce cerebral vascular resistance, reduce cerebral blood flow & CSF pressure.

Xanthine alkaloids inhibit cyclic nucleotide phosphodiesterase, thus prevents cyclic AMP to 5'AMP.

Uses: in Migraine, in acute left ventricular failure, bronchial asthma, as diuretic.

Doxapram used as respiratory stimulant in preanaesthetic period & in patients with hypoventilation. It is used to treat opioid induce post operative respiratory depression.

Medroxyprogesterone: It has respiratory stimulant action. It has been used with some success in patients with chronic ventilatory failure due to pathological condition.

ANTIPSYCHOTIC DRUGS

Classification:

a) Phenothiazine derivatives: Chlorpromazine
b) Rauwolia alkaloids: Reserpine
c) Butyrophenone derivatives: Haloperidol, Trifluperidol
d) Diphenhylbutyl piperidines: Pimozide, Penluperidol, Triluperidol
e) Thioxanthene derivatives: Chlorprothixene, Flupenthixol
f) Indolic derivatives: Molindone
g) Dibenzodiazepines: Clozapine
h) Substituted benzamides: Sulpiride
i) Miscellaneous: Oxypertine, Risperidone

Phenothiazines: These can cause blockade of postsynaptic monoaminergic transmission (dopamine, NA, 5-HT) in brain thus leading to a decrease in central sympathetic activity. It reduce incoming sensory stimuli by acting on brain stem reticular formation. It modify the function of mesolimbic system.

Uses: in Schizophrenia, maniac depressive psychosis. Chlorpromazine acts as antiemetic, antihiccup.

Raulwofia alkaloids produce depletion of endogenous catecholamines 5-HT from brain and peripheral sites.

Atypical antipsychotics: Clozapine, olanzepine, Risperidone.

Clozapine: Acts like phenothiazines except in that it causes fewer extrapyramidal reactions, does not cause hyperolactinemia.

Olazepine: Like clozapine greater 5-HT2 blockade than D2 receptors.

Risperidone: It has action on D2, 5-HT & alpha-adrenergic receptors.

ANTI ANXIETY DRUGS

Benzodiazepine: It facilitate the inhibitory presynaptic and/or postsynaptic action on GABA. It is used in anxiety, hypnotic, during withdrawal o anticonvulstants, anaesthetic medication.

Flumazenil: It binds competitively with benzodiazepine receptors & block many o pharmacologic actions of benzodiazepines. It will not block all pharmacological effects of GABA. It is used in benzodiazepine poisoning, Hepatic encephalopathy.

Meprobamate:

Chlorthiazole: In treatment of delirium tremens, used as an i.v. anaesthetic drug with Nitrous oxide. Hypnotic in elderly, in treatment of status epilepticus.

Buspirone: As potent as benzodiazepines but lacks sedative, hypnotic & anticonvulsant properties of benzodiazepines. It acts predominantly on 5-HT**1A** receptors resulting in an inhibition o dorsal raphae discharge. It has also affinity for D2 receptors.

Other Non Barbitures: Hydroxyzine, Diphenhydramine, Buclizine

ANTI DEPRESSNTS

Classification:

I. MAO inhibitors
   a) Hydrazine MAO inhibitors: Isocarboxazid, Iproniazid, Phenelzine
   b) Nonhydrazine MAO inhibitors: Tranylcypramine

II. Cyclic compounds
   a) Monocyclic: Toenacin

b) Bicyclic: Vilorazine
c) Tricyclic: Imipramine, Desipramine, Amitryptyline, Nortryptiline, Doxepin, Nitroxazepine, Clomipramine
d) Heterocyclic: Mianserin, Maprotiline, Trazodone

III. Selective Serotonin Receptor Inhibitors: Fluoxetine, Paroxetine, Fluvoxamine, Sertraline, Citalopram, zimeldine
IV. Miscellaneous: Carbamazepine
V. LiCO3

MAO Inhibitors: The enzyme Monoamine oxidase is present intracellularly in tissues. Its important function is to oxidize active biogenic amines like 5-HT, NA, Dopamine to inactive compounds. Inhibition of MAO-A decrease deamination of NA and to a lesser extent of 5-HT, and is associated with both antidepressant action and hypertensive interactions with foods containing Tyramine and with sympathomimetic drugs.

Tricyclic antidepressants: They inhiit reuptake & cause a localized increase in active NA in synaptic gap. They potent inhibitors o neuronal 5-HT uptake in brain. Can cause blockade of presynaptic alpha-2 adrenoceptors and also possess strong central anticholinergic properties. They used in mental depression, acute pain attacks, nocturnal enuresis, Bulimia nervosa.

LiCO3: Li increases rate of 5-HT synthesis in brain. It decrease the brain dopamine and NA synthesis and facilitate their neuronal reuptake. Used in Manic-depressive psychosis.

Carbamazepine: It is used as an alternative to Lithium in the prophylaxis of MDP in patients who do not tolerate/ do not respond to Lithium.

Sodium valproate: Substitute for or as an adjunct to Lithium in treatment of resistant cases of mania.

PSYCHOMOTOR STIMULANTS: Caffeine, amphetamine, Piperidyl derivatives like Pipradol, methylphenidate. They used in narcolepsy, cataplexy, in hypnogogic, sleep paralysis.

Drugs like Pemoline, methylphenidate used in attention deficit disorders.

DRUGS used in Parkinsonism

Classification:

I. Those that act through Dopaminergic system
a) Precursors of Dopamine: L-Dopa

b) Drugs that inhibit dopamine metabolism: Selegiline
c) Inhibition of COMT : Tolcapone
d) Drugs that release dopamine: Amantadine
e) Dopamine agonists: Bromocriptine, Apomorphine

II. Those that act through cholinergic system: Atropine, Benzhexole, Procyclidine.

Drug therapy for Extrapyramidal syndrome:

Tremors: Propranolol, Primidone

Chorea: Levodopa

Dystonias: Trihexyphenidyl, caramazepine, Diazepam

Myoclonus: Valproic acid, clonazepam

MOTOR NEURON DISEASE (MND) drug therapy:

Amyotrophic lateral sclerosis/MND is most severe degenerative neurological disorders. Glutamate is the principle excitatory amino acid neurotransmitter in the brain and spinal cord. Excessive stimulation of glutamate receptors may cause neuronal injury/death.

Ex: Riluzole, which blocks release of glutamate from neuronal cells, thus decreasing its extracellular concentration. Riluzole retards progression of MND.

Drugs used in Memory: Tacrine, which is an anti-cholinesterase, used in treatment of Alzheimer's disease. Donepezil, cholinesterase inhibitor.

LOCAL ANAESTHETICS

I. Natural: Cocaine
II. Synthetic Nitrogenous compounds:
    a) Derivative of PABA: Procaine, Amethocaine, Benzocaine, Orthocaine
    b) Derivative o Acetanilide: Lignocaine
    c) Quinoline Derivative: Cinchocaine
    d) Acridine derivative: Bucricaine
III. Synthetic Non-nitrogenous compounds: Benzyle alcohol, Propanediol
IV. Miscellaneous drugs: Clove oil, Phenol, Chlorpromazine

Mechanism of Action: Local anaesthetics blocks both generation and conduction of the nerve impulse. The blockade probably results from biochemical charges caused by the drug on the lipotropic film of cell membrane. The local anaesthetics like procaine prevent the increase in permeability of cell membrane to Sodium ion, in which is first event in depolarization, which leads to failure of propagation of an impulse without affecting the resulting potential, is known as membrane stabilizing effect.

Amethocaine – eye, throat, urethra, rectum, skin

Benzocaine & Lidocaine – all except eye

Dibucaine – ear, rectum, skin

Proparcaine – exclusively for eye only

Procaine – unsuitable for surface anaesthetic

AUTONOMIC NERVOUS SYSTEM

The ANS innervates the heart, smooth muscles, glands and the viscera. The structure receiving autonomic nerve supply possess an inherent physiological activity and the nerves influences only augment or reduce the initial functional level. ANS comprises two divisions Parasympathetic and Sympathetic. Both systems are in a state of dynamic equilibrium, the Parasympathetic system participate in tissue building reactions while sympathetic enables individual to adjust stress, prepare body for 'flight or fight'.

An animal can survive complete elimination of sympathetic system ut not of parasympathetic nervous system.

Parasympathetic Nervous System: Two functions

- Carries afferent impulses from viscera which reflexly modify autonomic functions
- Supplies motor fibres to smooth muscle, gland, heart and viscera through its craniosacral outflow.

Visceral afferents: These fibers are non-myelinated, mediate visceral sensations, regulate vasomotor, respiratory and viscerosomatic reflexes and coordinate the autonomic activity.

Neurotransmitters:

Acetylcholine: Acetylcholine is synthesized by combination of choline with acetyl group by enzyme choline acetylase. It is hydrolyzed by two main types of enzymes cholinesterases.

Sites of Action: a)All preganglion fibers of ANS, b)Post ganglionic parasympathetic nerve endings, c)sympathetic postganglionic nerve endings supplying sweat glands, d)somatic motor nerve ending, supplying skeletal muscles.

Noradrenaline & Dopamine: These act at post ganglionic sympathetic nerve endings & certain regions within the brain. Small portion of released NA metabolized outside the cell by COMT.

ADRENERGIC DRUGS

Classification:

I. Adrenergic drugs used for raising BP: *Noradrenaline, Metaraminol*
II. Those used for their inotropic action on heart: *Dopamine, Dobutamine, Isoprenaline, Xamoterol*
III. Those used as Central Stimulant: Amphetamine
IV. Those used as smooth muscle relaxant:
    a) Adrenaline, Isoprenaline, Isoxsuprine
    b) Selective Beta2-stimulants: Salbutamol
V. Those used in allergic reactions: Adrenaline, Ephedrine
VI. Those used for local vasoconstrictor effect: Adr, Naphazoline, Phenylephrine
VII. Those used or suppressing appetite: Fenfluramine, Phenteramine

Mechanisms of Action: Alpha receptor stimulation produce excitatory effects, beta receptor stimulation produce inhibitory effects. Noradrenaline acts on alpha receptors, Adrenaline acts both on alpha & beta receptors, Isoprenaline acts on beta receptors.

Beta adrenergic responses appear to result from binding of catecholamines to beta receptors (β1, β2) through G protein, stimulates the plasma membrane enzyme Adenylyl cyclase. This result is cAMP level.

- β1 receptors responsible for myocardial stimulation & renin release
- β2 receptors responsible for bronchial muscle relaxation, skeletal muscle vasodilation & uterine relaxation
- β3 receptors primarily in adipose tissue likely to regulate NA induced changes in energy metabolism & thermogenesis.
- α1 receptors increases intracellular concentration of Calcium ions by activation of Phospholipace C in cell membrane through G protein. Phospholipase causes hydrolysis of membrane bound phosphoinositides with generation of two second messengers diacyl glycerol, inositol triphosphate.

- α2 receptors inhibit adenylyl cyclase and reduce intracellular cAMP. Activation of α2 receptors in adrenergic nerves inhibit NA release whereas excitation of vascular α2 receptors causes release of EDRF which brings about vasodilatation.

Uses of Adrenaline: in treatment of anaphylactic shock, life saving in angioneurotic edema of larynx, used in acute attack of bronchial asthma, and in cardiac resuscitation.

Use of Noradrenaline: Mainly used or elevating P in shock.

Isoprenaline: Most powerul beta-receptor stimulant drug. It is used in treatment of bronchial asthma, stokes-adms syndrome, and in shock.

Adrenergic receptors:

α2	Medulla Oblongata	Reduction in BP & Heart Rate
α1	Blood vessels	Constriction (skin, cerebral)
α1	Sweat glands	Slight secretion
α1	Radial muscle of iris	Contraction (mydriasis)
α1	Sex organs, male	Ejaculation

β1	SA node	Increase heart rate
β1	Atria	Increase contration
β1	AV Node	Faster conduction
β1	Ventricles	Increased contractility
β2	Bronchial muscle	Relaxation
β2	Skeletal muscle	Changes in contractility
β2	Sk. Muscle bl vessels	Dilatation

EPHEDRINE: Alkaloid obtained from Ma Huang,It stimulates α,β receptors & release NA from sympathetic nerve endings. It is used as bronchial asthma, nasal decongestant, to treat hypotension during spinal anaesthesia, Stokes-Adams syndrome, as mydriatic, in urinary inconsistency.

Amphetamine: Adverse effects are addiction, paranoid psychosis, visual hallucinations.

NASAL DECONGESTS: Oxymetazoline, xylometazoline, propylhexedrine.

Selective β2 receptor stimulants: Orciprenaline, Salbutamol, Terbutaline, Ritodrine, Salmeterol.

Nylidrin: beta receptor stimulant, used in treatment of peripheral vascular disease.

Isoxsuprine: Potent inhibitory effect on vascular & uterine smooth muscle, used in treatment of dysmenorrhoea, threatened abortion, premature labor & peripheral vascular disease.

Adrenergic blockers (Alpha):

1. Beta haloalkyl amines: Dibenamine, Phenoxynenzamine
2. Natural dehydrogenated ergot alkaloids
3. Imidazoline derivatives: Tolazoline, Phentolamine
4. Quinazolines: Prazosin, Terazosin, Tremazosin
5. Miscellaneous: Indoramine, Yohimbine, Chlorpromazine

Dihydroergotamine is used to treat orthostatic hypotension, and in postpartum hemorrhage, and in abortion, where loss of foetus is inevitable, ergometrine employed to control bleeding.

Adrenergic Beta blockers:

I. Specific β-blocker: *Timolol, Nadolol*
II. β-blocker with membrane stabilizing activity & intrinsic sympathetic activity: *Oxeprenolol, Pindolol*
III. β-blocker with membrane stabilizing activity: *Propranolol*
IV. β-blocker with cardioselective action: *Acebutolol, Atenolol, Metoprolol, Esmolol*
V. β-blocker with additional α-blocking activity: Labetolol

Uses of Adrenergic Beta blockers: in Angina pectoris, myocardial infarction, cardiac arrhythmias, hypertension, thyrotoxicosis, pheochromocytoma, portal hypotension.

CHOLINERGIC DRUGS

Parasympathetic agents classified as:

a) Esters of choline: Acetylcholine, methacholine, carbachol, Bethanechol
b) Cholinomimetic alkaloids: Pilocarpine, muscarine, Arecholine
c) Cholinesterase inhibitors: Neostigmine, Pyridostigmine, Amenonium, Demecarium, Physostigmine,
d) Organophosphorous compounds

Acetylcholine has muscarinic action on gland cells, smooth muscle, and the heart while Nicotinic actions on autonomic ganglis, adrenal medulla, and motor end plates of skeletal muscles.

Acetylcholine increases gastric, intestinal & pancreatic secretions, bronchial, saliva, lacrimal & nasopharyngeal secretions also augmented. It decreases intraocular pressure & cause spasm of accommodation.

Acetylcholine increases adrenaline secretion, Acetylcholine induce contraction of skeletal muscles by keeping the muscle in depolarized state.

Cholinergic blocking drugs: Atropine & Hyoscine

Synthetic Morphine substitutes:

I. Mainly used in eye: Homatropine, Eucatropine, Cyclopentolate, Tropicamide, Dibutoline
II. Mainly used as spasmolytics:
Atropine – congenital hypertrophic pyloric stenosis
Methscopolamine – peptic ulcer, renal colic, frequency of micturition
Propantheline – relieving pain of diverticulitis, in diarrhea
Pirenzepine – Used for duodenal ulcers
Flavoxate – used to treat dysuria, nocturia, urinary urgency, suprapubic pain, prostatitis, urethritis
III. Other Quarternary ammonium compounds: Pipenzolate, clidinium, Procyclidin, glycopyrronium

SKELETAL MUSCLE RELAXANTS

Classification:

I. Drugs acting centrally: Baclofen, Mephenesin, Diazepam
II. Drugs acting peripherally at NMJ:
    a) Competitive block: d-tubocurarine, Botulinum toxin A
    b) Depolarization block: succinylcholine, decamethonium
III. Drugs acting directly on muscle: Dantrolene
IV. Drugs effective in Parkinsonis

HISTAMINE & ANTIHITAMINE DRUGS

Stimulation of H1 receptors produce smooth muscle contraction, increased vascular permeability and mucus secretion. It is associated with intracellular cyclic GMP.

Stimulation of H2 receptors increase gastric acid secretion, associated decrease in cGMP but increase in cAMP in cells.

Betahistine reduce frequency of episodes of vertigo. It causes vasodilatation & improve blood flow to labyrinth & brainstem.

H1 receptor antagonists:

I. Potent & Sedative: Diphenhydramine, Promethazine, Dimenhydrinate
II. Potent but less sedative: Triplennamine, Chlorcyclizine, Chlorpheniramine
III. Less potent & less sedative: Phenindamine, Mepyramine, Pheniramine
IV. Non-sedatives: Terenadine, Loratadine, Astemizole, Cetirizine

CHEMICAL Classification:

I. Ethanolamine derivatives: Diphenhydramine, dimenhydrinate
II. Ethylenediamine derivative: Triplennamine, Mepyramine, Antazoline, Methapyrilone
III. Alkylamine derivative: Chlorpheniramine, Triprolidine
IV. Piperazine: Chlorcyclizine, Meclizine, Cinnarizine
V. Phenothiazines: Promethazine, Methdilazine, Trimeprazine
VI. Piperidines: Astemizole, Terfenadine
VII. Miscellaneous: Phenindamine, Cetirizine, Acrivastine

5-HT & its antagonists

5-Hydroxytryptamine (Serotonin) present in tissues, mast cells & platelets. 5-HT is a constrictor of majority of blood vessels including renal, splanchnic & pulmonary arteries. 5-HT has weak direct positive ionotropic & chronotropic effects on myocardium.

5-HT antagonists: Methysergide, cyproheptadine, pizotifen, ketanserin, ondanserton.

Methysergide: Congener of LSD, used in migraine.

Cyproheptadine: 5-HT2 antagonist, it increases appetite. It is used in relief of pruritus, urticarea, in treatment of postgastrectomy dumping syndrome & carcinoid syndrome; symptomatic relief in seasonal & perennial pollinosis, as an appetite stimulant in certain conditions.

Pizotien: Used in Migraine & other vascular headaches.

Ondaserton: 5-HT3 antagonist used in vomiting.

DRUGS USED IN COUGH

I. Those acting as pharyngeal demulcent & local sialogogues: Syrups & linctusts
II. Those which increase respiratory tract fluid: Ex Expectorants
III. Those which act as central cough suppressants

Expectorants: Expectorants can stimulate the output o respiratory tract fluids either directly/reflexly.

Direct acting: volatile oils like eucalyptus oil, anise, lemon; Friar's Balsam

Reflex Expectorant: Ipecacunha

Saline Expectorants: Ammonium salts, potassium salts, potasium citrate, vasicine.

CENTRAL COUGH SUPPRESSANT

I. Opioids: Codeine, Noscapine & dextromethorphan
II. Antihistamine antitussives: Diphenhydramine, Chlorcyclizine, Dimethoxanate
III. Benzonatate
IV. Miscellaneous: Piperidone, ethyl dibunate, Pimetine

Mucolytic Agents: Acetyl cysteine, Bromhexine, Pancreatic dornase

DRUGS Used in ASTHMA

I. Bronchodilators
   a)Sympathomimetics: Adrenaline, Ephedrine, Isoprenaline, Orciprenaline, Salbutamol, Terbutaline, Famoterol, Salmeterol
   b)Theophylline & its derivatives
   c) anticholinergics: Ipratropium

II. Drugs acting by interacting with leukotriens
   a) LT syntheis inhibitor: Zileuton
   b) LT receptor antagonists: Monteleukast
III. Antiiflammatory drugs: Corticosteroids, sodium cromoglycate
IV. Antihistaminics: Ketotifen

Drugs for Chronic Persistent Asthma: Beclomethasone, Budesonide

DRUGS USED IN CARDIAC FAILURE

I. Digitalis: used in Congestive cardiac failure, Left Ventricular failure
II. Ouabain
III. Amrinone

Vasodilators in Congestive Cardiac Failure (CCF):

- Arterial: Hydralazine, Minoxidil
- Venous: Nitrates
- Combined, Balanced arteriolar + Venous: Prazosin, Phentolamine, Nitroprusside

DRUGS USED IN CARDIAC ARRHYTHMIAS

I. Sodium channel blockers
   a)those prolong depolarization: Quinidine, Procainamide, disopyramide
   b)those which shorten repolarization: Lignocaine, Phenytoin, Mexiletine, Tocainide
   c)those which have no effect on action potential duration but on phase '0' depolarization rate: Flecainide, Propafenone

II. Beta adrenergic blockers: Propranolol
III. Potassium channel blockers: Amiodarone, Brotylium, Sotalol, Cordarone
IV. Calcium channel blockers: Verapamil, Adenosine, Bretylium
V. Digitalis

Drugs used in treatment of Heart Block: Isoprenaline

ANTIHYPERTENSIVE DRUGS

I. Drugs acting centrally
   a)α2-adrenergive receptor stimulants: Clonidine, methyldopa
   b)selective imidazole receptor stimulant: Moxonidine

II. Drugs acting on autonomic ganglionic blocking agents: Hexamethonium & Trimethophan

III. Drugs acting on postganglionic sympathetic nerve endings:
a)Adrenergic neurone blockers: Guanethedine, Bethonidine, Bretylium, Debrisoquine
b)Catecholamine depletors: Reserpine

IV. Drugs acting on adrenergic receptors:

a) α-adrenergic blocking: Phentolamine, Phenylbutazone, Prazosin, Indoramine
b) β-adrenergic blocking: Propranolol, Atenolol, Metoprolol
c) Both α & β blocking: Labetolol

V. Drugs acting directly on vascular smooth muscle:

a)Arteriolar vasodilators: Hydralazine, Diazoxide, Minoxidil
b)Arteriolar-venular vasodilator: Sodium nitroprusside

VI. Potassium channel activators: Minoxidil, Nicorandil, Diazoxide

VII. Drugs acting reflexly by stimulating baroreceptors: Veratrum

VIII. Drugs which block renin-angiotensin-aldosterone axis:
a)which block renin release: Beta adrenergic blockers
b)ACE inhibitors: Enalapril, Captopril, Perindopril
c)Those which competitively block Angiotensin II at vascular receptor sites: Salarasin, Losartan
d)Aldosterone antagonist: Spiranolactone

IX. Oral Diuretics: Thiazide

X. Miscellaneous: Metyrosine

DRUGS USED IN ANGINA PECTORIS

I. Organic nitrates: Glyceryl trinitrate, Isosorbide dinitrates
II. Beta adrenergic blocking agents: Atenolol, Bisoprolol, Metoprolol
III. Calcium channel blockers: Verapamil, Diltiazem, Nifedipine, Amlodipine
IV. Potassium channel activators: Nicorandil

V. Antiplatelet drugs: Aspirin, Dipyridamole
VI. Cytoprotectives: Trimetazidine

Drugs decrease platelet aggregation: Aspirin, Prostacyclin (PGI2), Dazoxiben, Dipyridamole, Ticlopidine, Pentoxyfylline.

ANTICOAGULATNS:

I. Those used or preventing clotting of blood inside in vasculature
a)Rapidly acting: Heparin
b)Slow acting: Coumarin derivativges, Indane dione derivative (Phenindione)
c) Warfarin

Some low molecular weight Heparins: Enoxaparin, Dalteparin, Tinzaparin, Parnaparin, Reviparin

- Heparin Antagonist = Protamine sulphate

Thrombolytic Agents: Streptokinase, Alteplase, Urokinase,

Agents Used for Control Bleeding: Thrombin, Fibrin, Oxidized cellulose, Microfibrillar collagen hemostat, fibrinogen, antihaemophilic globulin, vitamin c + Rutin, Vitamin K, Epsilon aminocaproic acid, Tranexamic acid.

DIURETICS

I. Weak Diuretics
a)Osmotic Diuretics: Electrolytes like Na, K salts; Non electrolytes like Mannitol, isosorbide, sucrose, glycerol
b) Acidifying salts: Ammounium chloride, Arginine Hydrochloride
c)Xanthine derivatives: Aminophylline
d)Carbonic Anhydrase inhibitor: Acetazolamide

II. Moderately Potent Diuretics: Chlorthalidone, Chloroxolone, Clopamide

III. Very Potent Diuretics (High Ceiling): Furosemide, Bumetamide & ethacrynic acid, organic mercurial compounds

IV. Potasium sparing diuretics: Triamterone, Amiloride, Spiranolactone

Digestants: Pepsin, Renin, Pancreatin, Bile salts, Chenodeoxycholic acid, Ursodeoxycholic acid, Takadiastase.

Chenodeoxycholic acid is used for treatment of gall stones.

CARMINATIVES: Dimethylpolysiloxane, used in treatment of postprandial & post operative flatulence & abdominal distension

APPETITE SUPPRESSANTS:

I. Centrally acting: amphetamine, dexamphetamine, Dextroamphetamine
II. Bulk anorexiants: Methyl cellulose, Karaya gum, glucomannon

HYPOLIPIDEMIC DRUGS

I. Drugs act on elevated Triglycerides: Fibric acid derivatives gemfibrogil, clofibrate, Fenofibrate
II. Drugs act on elevated cholesterol: Cholestyramine resin, HMG CoA inhibitors, estrogen, Probucol
III. Both on TG & cholesterol: Nicotinic acid.

Fenofibric acid derivatives: These drugs stimulate lipoprotein lipase activity & hydrolysis of TG in plasma. They reduce the incorporation of fatty acids into VLDL in liver, thus inhibiting the synthesis & secretion of VLDL.

Cholestyramine Resin: It binds the cholates into an insoluble complex which is excreted in faeces. Prevention of cholate reabsorption leads to a marked increase in their synthesis from plasma cholesterol & consequent reduction in serum LDL cholesterol levels.

Colestipol acts as above.

HMG CoA reductase Inhibitors: Ex Atrovastatin, Rosuvastatin, Simvastatin

Estrogens: Treatment of postmenopausal women with conjugated estrogen accelerate LDL catabolism but TG rich VLDL increases.

Gugulipid:

Nicotinic Acid: Large doses of Nicotinic acid effectively and rapidly reduce plasma TG concentration by lowering VLDL levels.

EMETICS

I. Centrally acting by stimulation of CTZ: Apomorphine, Morphine, Hydergine
II. Peripherally acting: Mustard, Antimony & Potassium tartrate, hypertonic Sodium Chloride
III. Both peripherally & centrally acting: Ipecacunha

ANTIEMETICS

I. Antidopaminergics: Chlorpromazine, Metaclopramide, Domperidone
II. Antihistaminics: Cyclizine, Meclizine, Promethazine, Dimenhydrinate
III. Anticholinergic: Scopolamine
IV. Anti 5-HT: Ondanserton, Graniserton
V. Miscellaneous: Nabilone, Cisapride,Trimethoenzamide

DRUGS used in Vertigo & Dizziness: Antihistaminics like Cinnarizine, Flunarizine, Dimenhydrinate, Hydroxyzine.

DRUGS USED IN DIARRHOEA

Agents useful against diarrhea may include:

i. Act locally as protecting by coating the gut: Bismuth salts, Prepared chalk, light kaolin, Pectin
ii. Decreasing propulsion of intestinal contents: Codeine,Tincture of opium, diphenoxylate, paregoric, Loperamide
iii. Act on intestinal microcirculation: PG Inhibitors like Indomethacin, Aspirin
iv. Act directly on mucosal transport process: Lactobacillus acidophilus, Berberine

DRUGS USED IN CONSTIPATION

I. Stimulant/irritant laxatives:
   a)Anthraquinone group: Cascara, senna
   b)Irritant Oils: Castor oil
   c)Miscellaneous: Phenophthalein, Bisacodyl, Sodium picosulphate

II. Osmotic Laxatives: $MgSO_4$, Milk of Magnesia, Mg citrate, Potassium Sodium tartrate, Lactulose, PEG
III. Bulk Laxative: Methyl cellulose, Agar Agar, Plantago seeds, Bran
IV. Emollient Laxatives: Liquid paraffin, Dioctyl Sodium sulfosuccinamate

DRUGS USED IN PEPTIC ULCER

I. Gastric antacids
   a)Non Systemic: Aluminium hydroxide gel, Mg trisilicate, Magnesium hydroxide, MaO, $CaCO_3$
   b)Systemic: $NaHCO_3$

II. Gastric acid secretion inhibitors:
   a)Antimuscarinic: Pirenzepine
   b)H_2 Antagonists: Cimetidine, Ranitidine, Famotidine
   c)Proton pump inhibitor: Omeprazole, Pantaprazole, Esomeprazole etc.

III. Miscellaneous: Bismuth salts, sucralfate,
IV. Analogues of Prostaglands like PGE1 (Misoprostal), PGE2 (Emprostil, Rioprostil)

OXYTOCIC & UTERINE RELAXANTS

I. Ergot Alkaloids: Ergometrine (used in postpartum hemorrhage, Uterine involution, Orthostatic hypotension)
II. Oxytocin: It released from posterior pituitary gland, used in induction of term labor, uterine inertia, postpartum hemorrhage, Abortion
III. Miscellaneous:
a)Prostaglandins: Dinoprost, Carboprost, Gemeprost.
b)Hypertonic Saline
c)Urea
d) Ethacrine lactate

UTERINE RELAXANTS (TOCOLYTICS)

Salbutamol, Ritodrine, Orciprenaline, $MgSO_4$, Relaxin

SULFONAMIDES

Mechanism of Action: These exhibit structural similarity to para amino benzoic acid (PABA). They compete with and substitute for bacterial metabolism. Folic acid derived from PABA is important in bacterial metabolism. Sulfonamides inhibit enzyme folic acid synthetase which is involved in conversion of PABA to folic acid.

Uses: in treatment of Urinary tract infections,acute bacillary dysentery, meningococcal meningitis, Ulcerative colitis (Mesalazine, sulfasalazine), chancroid, toxoplasmosis etc.

COTRIMOXAZOLE: Combination of trimethoprime and sulphonamide gives synergistic results against most bacteria. Trimethoprime acts by inhibiting Dihydrofolate reductase, necessary for conversion of dihydrofolate to tetrahydrofolic acid.

QUINOLONES: Ex. Nalidixic acid, they inhibit bacterial DNA gyrase, leadijng to interference with synthesis of nucleoproteins.

Fluoroquinolones: These act same as quinolones ex: Ciprofloxacin, Norfloxacin, Ofloxacin, Lomefloxacin.

ANTIBIOTICS Classification:

I. Effective against Gram Positive Bacteria
   a)Systemic infection: Penicillins, Macrolides, Fucidin
   b)Topical: Bacitracin

II. Mainly effective against Gram Negative Bacteria
   a)Systemic: Streptomycin and other aminoglycosides
   b)Local: Paromomycin

III. Effective on both:
   a)Systemic: Ampicillin, Amoxycillin, carbenicillin, Imipenam
   b)Topical: Neomycin, Framycetin

IV. Effective against both and Rickettsiae & Chlamydia: Ex: Tetracyclines, cholramphenicol

IV. Effective against acid fast bacilli: Streptomycin, Rifamycin, kanamycin, capreomycin

V. Effective against Protozoa: Paromomycin, Tetracycline

VI. Effective against Fungi: Nystatin, Amphotericin B, Griseofulvin

VII. Antimalignancy: Actinomycin D, Mitomycin & Azaserine

PENICILLINS:

Mechanism of Action: Peptidoglycan is structural component of bacterial cell wall that is cross linked into net like structure that surrounds cell. Penicilin binding proteins are bacterial enzymes are responsible for synthesis of peptidoglycan in cell & penicillin penetrate bacterial cell wall & inactivate them. This weakens the cell wall.

Probenecid along with penicillin, increase plasma level of penicillin to 2-4 fold.

Adverse effects: Allergy, Anaphylactic shock, Hyperkalemia

Semisynthetic Acid Resistant Penicilins: Penicillin V, Azidocillin

Penicillinase resistant Penicillin: Methicillin, Nafcillin, Cloxacillin,

Penicillins effective Gram +ve, -ve : Ampicillin, Talampicillin, Amoxycillin

Extended spectrum penicillin: Carbenicilin, Ticarcillin, Piperacillin, Mecillinum

Clavulanic acid: Produced by Streptomyces clavuligreus, given with Amoxycillin, ticarcillin. It is potent beta-lactamase inhibitor.

Macrolides: Ex Erythromycin, spiramycin, Azithromycin, Clarithromycin. These act by inhibiting protein synthesis by binding to 50s ribosomes.

Lincomycin: Obtained from Streptomyces lincolensis

Vancomycin: Obtained from Streptomyces orientalis

Sodium Fusidate (Fucidin): Obtained from Fusidium coccineum

Bacitracin: Obtained from Bacillus subtilis, which is a polypeptide.

Mupirocin: Obtained from Pseudomonas fluorescens.

AMINOGLYCOSIDES

Mechanism of Action: These penetrate outer cytoplasmic membrane & inhibit protein synthesis. The ribosomes manufacture enzymes under the direction from mRNA. They combine with bacterial ribosomes, interfere with mRNA-ribosome combination.

Streptomycin: Obtained from Streptomyces griseus

Kanamycin: Streptomyces kanamyceticus

Gentamicin: Obtained from Micromonospora purpura

Tobramycin: Obtained from Streptomyces tenebrarius

Neomycin: Obtained from Streptomyces fradiae

Framycetin: Obtained from Streptomyces decaris

Paromomycin: Obtained from Streptomyces rimosus

NON AMINOGLYCOSIDES AGAINST GRAM NEGATIVE Organisms:

Colistin: Obtained from Aerobacillus colistinus

Polymyxin B

Tyrothricin: Obtained from Bacillus brevis

Cycloserine: Obtained from Streptomyces orchidaceus

Spectinomycin: Obtained from Streptomyces spectabilis

Monobactam: Aztreonam.

CEPHALOSPORINS

Cephalosporins have 7-Amino cephalosporanic acid nucleus which resemblance to 6-Amino penicillanic acid of Penicillin.

Mechanism of Action: They inhibit bacterial cell wall synthesis.

Carbapenems: Ex Imipenam, Meropenam, These are beta lactam antibiotics. Imipenam given along with cilastatin to protect from Dipeptidase enzyme produced by kidney.

Rifamycin: Obtained from Streptomyces mediaterranei.

TETRACYCLINES

Mechanism of Action: The susceptible bacteria accumulate tetracycline by active transport system. Tetracyclines interfere with protein synthesis by blocking attachment of aminoacyl transfer RNA to acceptor site on mRNA ribosome complex.

Adverse effects: Allergy, Photosensitivity, Fanconi like syndrome on kidney

Semisynthetic Tetracyclines: Ex: methacycline, doxycycline, minocycline

Uses: Rickettsial infection, cholera, chlamydial infection, primary atypical pneumonia, granuloma inguinale, brucellosis, Urinary tract infections, in sexually transmitted diseases, plague, Acne vulgaris, leprosy etc.

Chloramphenicol: Obtained from Streptomyces venezulae. It rapidly penetrates into cell and acts by interering with synthesis of bacterial proteins by inhibiting 50s ribosomes.

Adverse effects: Gray Baby syndrome, Bone marrow toxicity.

ANTIFUNGAL AGENTS:

I. Topical: Nystatin, Pimaricin, Hamycin
II. Systemically:
a)antibiotics: Griseofulvin, Amphotericin B
b)Antimetabolite: Flucytosine
c)Azole derivatives: Clotrimazole, Miconazole, Ketoconazole
d)Miscellaneous: Terbinafine

Nystatin: Obtained from Streptomyces noursei

Griseofulvin: Obtained from Streptomyces nodosus

Azoles: They act by inhibiting synthesis of ergosterol which is present in fungal cell membrane.

DRUGS USED IN TUBERCULOSIS

I. Standard Drugs:
a)Bactericides: Isonicotinic acid Hydrazide (INH), Rifampicin, streptomycin, Pyrazinamide
b)Bacteriostatic: Ethambutol, Thiacetazone

II. Reserve Drugs:
a)Bactericidal: Capreomycin, Kanamycin, Fluoroquinolone
b)Bacteriostatic: Ethionamide, Cycloserine, Paraamino salicylic acid

D
DRUGS USED IN LEPROSY

I. Sulfones: Dapsone

II. Riampicin
III. Clofazimine
IV. Ethionamide
V. Ofloxacin, Clarithromycin

ANTIMALARIAL DRUGS

I. Cinchona alkaloids: Quining
II. 4-Aminoquinolines: Chloroquine, Hydroxy chloroquine, Amodiaquine
III. 8-Aminoquinolines: Primaquine
IV. Acridines: Mepacrine
V. Biguanides: Proguanil
VI. Diaminopyrimidines: Pyrimethamine
VII. Quinoline methanol: Mefloquine
VIII. Phenanthrene methanol: Halofantrine
IX. Miscellaneous: Sulfonamides, Tetracyclines & Quinghosu

DRUGS USED IN AMOEBIASIS

I. EMETINE Group: Emetine (Luminal amoebicidal)
II. Quinoline derivative: Chloroquine, di-iodo hydroxyl quinoline (Extra intestinal amoebiasis)
III. Imidazole derivatives: Metronidazole, Tinidazole, secnidazole (tissue amoebicide)
IV. Antibiotics: Tetracyclines, Paromomycin
V. Miscellaneous: Diloxanide, Niridazole, Kurchi

Drugs used in Tapeworm infection: Niclosamide, Praziquantel, Chloroquine, Amodiaquine, Mebendazole

Drugs used in Roundworm infection: Piperazine, Pyrantel, Levamisole, Mebendazole, Albendazole

Drugs used in Hookworm infection: Biphenium hydroxynapthoate, Mebendazole, Pyrantel

Drugs used in Pinworm infection: Mebendazole, Pyrantel, Viprynium or pyrivinum, Piperazine, Gential violet

Drugs used in Filariasis: Diethyl carbamazepine (DEC), Ivermectin

ANTINEOPLASTIC DRUGS (CANCER DRUGS)

I. Alkylating agent
   a)Nitrogen mustards: Mechlorethamine, Cyclophosphamide, Melphalan, Chlorambucil
   b)Ethyleneamine: Thiotepa (Triethyl thiophosphamide)
   c)Alkyl sulonates: Busulfan

II. Antimetabolites:
   a)Folic acid antagonists: Methotrexate
   b)Purine antagonists: 6-mercaptopurine, Azathioprine
   c)Pyrimidine antagonist: Fluorouracil, cytosine arabinoside, Fluorodeoxy uridine

III. Radioactive isotopes: Radioiodine,Radiogold,Radio phosphourous
IV. Cytotoxic antibiotics: Actinomycin D, Mitomycin C, Bleomycin, Mithromycin
V. Antimitotic plant products: Vinblastine, Vincristine, Taxol
VI. Hormones & Hormone antagonists: Tamoxifene, flutamide, GnRH antagonists
VII. Miscellaneous: Cisplatinum, Procarbazine
VIII. Biological response Modifiers: Interferons, BCG, Levamisole.

CYTOLOGY: The structural and functional unit o all the living organisms is called Cell. The shape and size of the cells are not only different for various organisms but the cells are also different in the same organism of different organs. The cell was firstly discovered by Robert Hooke. J.E. Purkinje point out that life saving substance is protoplasm. Further protoplasm is also of two types – Cytoplasm and Nucleoplasmk. Cytoplasm is confined between nucleus and cell membrane, while Nucleoplasm is confined inside cell membrane.

Cell Theory: Cell theory was proposed by Schleiden & Shwann, according to the theory: Every organism originates from cell, the body of every organism is made of one or more cells, the process through which the cell is formed has a complex mechanism but the core of the cell is nucleus.

CELL STRUCTURE: The cell is basically made of various layers called cell organelles.

Cell Membrane: The cell membrane of the cell is an outer layer of the cell and it is basically a semipermeable membrane. This membrane is live and semipermeable because all cellular substances are not allowed to pass through it. This membrane looks like a double membrane in which various holes are appeared. Basically the cell membrane is made of lipid and protein in which between a layer of two identical layer's o proteins are confined. It also provide mechanical support to cell. In animal cells the cell membrane helps in the formation of cilia, flagella, microvilli etc.

Cell Wall: The cell wall is only found in the plant cells. The cell wall is made of a non-living substance. This non-living substance is hard and thick membrane which is cellulose. The cellulosed is basically a complex substance which provide a structural support to the cell. The cell walls of bacteria and fungi are made of carbohydrates. The main function o cell wall is to protect nucleoplasm and cell membrane from external invasion.

Nucleus: The nucleus of the cell wall invented by Robert Brown in 1831. The nucleus present near the cellular centre of the cell. This is controlling centre of almost all activating take place inside the cell. There are various components of the nucleus o the cell like nucleus membrane, nucloplasm, nucleolus, nuclear network etc.

Nucleus Membrane: The nucleus membrane is made of two layer's membrane surrounded which nucleus o the cell is surrounded. The outer layer is connected through endoplasmic reticulum of the cell. Nucleus membrane is made up of proteins and lipids.

Nucleoplasm: The nucleoplasm is the protoplasm of the inside nucleus of the cell. The nucleoplasm is made of proteins, phosphorous and nucleic acids which are abundantly found in it.

Nucleolus: The condensed part of nucleus is called nucleolus. The main function of nucleolus is to synthesize r-DNA, to assist the synthesis of r-RNA and in transportation of it, to collect ribosome inside the nucleolus.

Nuclear Network: The main body of the nucleolus is like a network structure in which thick particles are found which is called chromatin. Chromatin is a genetic substance found in the cell and it is basically composed of Histone protein, DNA and RNA. During cell division, chromatin is compressed and divided into various smaller thick and consolidated form and these are called chromosomes.

Chromosomes: Chromosomes are the basic constituents of a genetic substance chromatin and in every chromosome there exists a dense jelly like substance called matrix and in two mutually thin interconnected coiled shaped structures seems to appear which is called chromonemata. Every chromonemata is called chromatid, thus every chromosome is composed of two chromatids.

These chromatids met a place which is called centromere. On chromosomes various genes are located and this gene is a functional unit of DNA. The characteristics which transmit from generation to generation is transported by genes.

DNA & RNA: DNA means De-oxyribose Nucleic acid and RNA means Ribonucleic acid. DNA is a polynucleotide and is confined in the nucleus of the cell, very small amount present in mitochondria and green plastids.

Watson & Crick proposed DNA as Double Heliz. This double helix are the opposite parallel direction and each helix has a diameter or nearly 20°A. DNA regulates genetic activities and its basic unit is gene. It also regulates protein synthesis.

RNA is single stranded but in some viruses it has double stranded structure. The main function of RNA is to assist in protein synthesis but in some plants & viruses it acts like a carrier of genetic substance. RNA is of three types:

r-RNA (Ribosomal RNA): It is attached on ribosome and helps in protein synthesis and it forms from DNA in the nucleus of cell and constitute 80% of the total RNA.

t-RNA (Transfer RNA): It brings all types of amino acids on the ribosome where protein is formed. It constitute 10-15% of total RNA and it is the smallest among all. It has two dimensional structure like clove leaf.

m-RNA (Messenger RNA): It carries information of the protein synthesis from DNA of the nucleus to ribosome. It constitute 3-5% of all RNA. It also helps selecting amino acids.

Cytoplasm: Various organells like endoplasmic reticulum, golgi apparatus, lysosome, mitochondria, centrosome, plastids,chromoplast, chloroplast etc and organic and inorganic substances present in cytoplasm.

Endoplasmic Reticulum: ER is spread between cell membrane and nuclear membrane in the cytoplasm. ER is basically made of lipoproteins which are core of fat and cholesterol along with a lipid membrane. Two types of ER present. Smooth walled ER have no ribosome found and it is respondent for the lipid secretion. Rough walled ER contains ribosomes and helps in protein synthesis.

Golgi Apparatus: It composed of tubules and vesicles. Golgi apparatus has complex structure through which the proteins are synthesized and other substances are processed in the form of package and the packages are brought to their destination. It is called traffic controller of cellular molecule.

Lysosomes: It is composed of membrane in the form of a packet which is found in every cell. In lysosome there is powerful hydrolytic enzyme lysozyme present which is able to digest every organic substance. This is called suicide vesicle of the cell.

Mitochondria: In mitochondria, so many respiratory enzymes are present. It is elliptical shape and is a semi autonomous organelle surrounded by two membranes. The external membrane is smooth, while inner membrane forms finger shaped matrix is called tubuli for the plant cells and cristae for animal cells. This is called Power House of the Cell.

Ribosome: It is composed of RNA and protein and its main function is to synthesize the protein, so it is called factory of protein.

Centrosome: Centrosome helps in cell division and it form spindle fibre. In animal cells near the nucleus there is brightened small are in the centrosome which is called centreole.

Plastid: Only found in the plant cells and is shape is like mitochondria. It has two membranes but not present cristae. Three types of plastids present, these are

a) Leucoplast: This is found in the cells o those parts of the plant which are deprived from sunlight like roots, underground stems etc. It contains oil drops, starch.
b) Chromoplast: This is colored plastid which has usually red, yellow or orange color. It is found in flowers, interior of fruits, seeds etc. Ex Lycopene (tomato), carotene (Carrot), Betanin (Beet root) etc.
c) Chloroplast: This is made of a green colored substance chlorophyll in which Magnesium is present. By chlorophyll, the photosynthesis is completed in presence of sunlight and produce glucose. So it is called Kitchen of the cells.

Vacuoles: Vacuoles are surrounded by semi permeable membrane which is called Tonoplast and main function of vacuoles are to collect the food stuffs in which mineral salts, sugar, CO_2, Oxygen, organic acids, various colors are dissolved. Vacuoles help in transportation of various cellular substances inside the cell. The plant vacuoles are filled up with cell sap which basically a non-living substance. Some specific vacuoles of unicellular organisms help to expel the residual substances from the bodies.

Microtubules: In the cytoplasm of the cells small tubules like structures are found which are called microtubules. The microtubules play significant role during cell division and participate in spindle formation.

- The smallest cell is Mycoplasma Gallopsepticum, Largest cell is Ostrich's egg and Longest cell is Neuron.

On the basis nuclear composition of the cell, there two types of cells.

i)**Prokaryotic cell**: These cells are called primitive cells because structures of such cells are very simple. The chromosome made of the genetic material DNA is present in specific area of cytoplasm and is called nucleoid. It lacks nuclear membrane. Many organells like mitochondria, golgi complex, ER are absent.

ii)**Eukaryotic cell**: Cell all around nucleus have developed nuclear membrane is found and the cell contains mitochondria, gogli complex, ER etc. In eukaryotic cells, cell wall is completely developed and which is composed of cellulose. Animal cells do not contain it.

CELL DIVISION

Old cells split into new cells and the formation new cells, is called cell division. Cell division is of three types Amitosis, Mitosis and Meiosis.

Amitosis: This type of cell division takes place in a less developed cell of unicellular organisms and in this division firstly the nucleus of the cell is divided and later the cytoplasm is divided and ultimately two new cells are formed. It is present in bacteria, blue green algae, yeast, amoeba, protozoa etc.

Mitosis: It is also called somatic cell division and in such type of cell division two identical cells are produced. In mitosis cell is divided but number of chromosomes are remain the same and mitosis is a continuous process.

i) **Prophase**: In all animal cells and in the cells of some plants like of fungi and some algae, centriole duplicates itself and divides in such a way that the two new centrioles move to the opposite ends of the cell. A series of fibres come from

centriole towards nucleus. The chromosomes will shorten and thick. The nucleus and nuclear membrane begin to disintegrate in the late prophase.

ii) **Metaphase**: The pairs of chromosomes align themselves in such a way that the centre of the cell and each centromere becomes attached to one spindle fibre from each pole. The centromere divides and the separated chromatids become independent daughter chromosomes.

iii) **Anaphase**: The daughter chromosomes move apart from each other and migrate to the opposite poles. As the daughter chromosomes move towards the poles, the spindle fibres are shorten.

iv) **Telophase**: As the daughter chromosomes reach the poles, now the spindle fires totally disappear and a nuclear membrane forms around each new group of chromosomes.

v) **Cytokinesis**: After the division of nucleus, cytoplasm starts to divide and the original larger cell becomes two smaller identical cells and each daughter cell takes food, grows, being divided and the process continues.

Significance o Mitosis: In mitosis two similar daughter cells are formed through single mother cell. Because of this cell division the number of chromosomes in all formed daughter cells are same. In all living organisms growth take place due to this cell division.

MEIOSIS: It consists of two successive cell division that resembles like mitosis but the chromosomes are duplicated only once. Thus gametes have half the number of chromosomes normally found in the body cells. There are two sub stages – Meosis I and Meosis II. During Meosis I, the number of chromosome is reduced to hal so that the diploid nucleus gives rise to two haploid ones.

In Meiosis II, there is no reduction in the number of chromosome and the haploid nuclei divided mitotically to produce four haploid daughter nuclei. Thus from every diploid nucleus which undergoes meosis four haploid nuclei are formed.

The exchange of segments of chromosomes which takes place during meosis I, is responsible for the interchange of genes, genetic recombination and the process is called crossing over.

Significance of Meiosis:

- During cell division, sex cells are formed through the sperm and ovum in which the number of chromosomes are halved. The sex cells are unique to organisms which reproduce sexually in formed somatic cells after fertilization again the number of chromosome are diploid which are as usual of mother cells.

- During meiosis chromatin substances present in the cell are mutually exchange themselves. Due to it the possibility of genetic characters of father & mother strongly appear in their offsprings.

VIRUS

Virus is micro organism which is found in the form of parasite in the living cells of the organism. Viruses were discovered by Dimitri Ivanovsky.

Characteristics of Viruses:

- Lack of cellular level composition like cytoplasm, cell membrane, cell organelles etc in the virus.
- Inside the plants viruses transmit through phloem, while inside the animals transmission takes place through the blood of the body.
- Viruses have either DNA or RNA but both are never present.
- Viruses exhibit the properties living and non-living.

PLANT HORMONES

The plant hormones are prepared by the apical meristem younger mature leaves and transported through the vascular tissue phloem to the other organs of the plant. The plant hormones are: Auxins, Gibberellin, Cytokinins, Ethylene, Abscisic acid, Calins, Florigens etc.

Auxins: It causes cell division and cell elongation consequently a sustained growth takes place in plants. By this hormone, seedless fruits are produced. This hormone is used as weedcide as it is spread in the fields of crops of wheat and then toxic weeds which appear along with these crops are completely destroyed.

Parthenocarpy: If some hormone auxin is applied on the flower of the plants then without fertilization and without seeds formation the wall of ovary becomes tuberous and forms fruit.

Gibberellins: It is formed at the most elevated part of the stem column, new leaves and seeds of the plants. The hormone is used for increasing height of plant. By the use of gibberellins the time taken in blossoming the flowers and the fruit formation time can be reduced. Gibberellins active the process of cambium in wood plants.

Cytokinins: It activates the rate o cell division. It activates the passive tissues of the buds of seeds and stems for a substantial growth. The activity of mutation can be stopped by the use of Cytokinins.

Ethylene: Ethylene is the only gaseous hormone which is a growth controller. It is used for fruit riping. By the use o this hormone the number of female flowers can be increased. This hormone also activates the abscissional activities of leaves, flowers and fruits.

Abscisic acid: It activates the vascular cambium during mitosis cell division and its presence slows down the stems growth. The hormone prevents sprouting activities in seeds and buds. In dry stems it activates the pores to close and consequently a downfall in the rate of evaporation takes place.

ANATOMY & PHYSIOLOGY

TISSUES

The branch of biology under which the tissues are studied is called Histology. Almost all higher animals including human beings are four types of tissues and these are: Epithelial tissues, Connective tissue, Muscular tissue, Nervous tissue.

EPITHELIAL TISSUE: The epithelial tissues forms a continuous layer over the free surface of many other tissues. It covers the external surface of the animal body, internal surfaces of visceral organs, body cavities and blood vessels. Linings of some hollow organs or cavities are moist because of mucus secreted by epithelial tissue. Blood vessels are absent epithelial tissue. The epithelial tissue classified into Simple and compound Epithelia.

A)Simple Epithelia: It is formed from a single layer of cells, resting on the basement membrane. Various types of simple epithelia are:

i)Squamous epithelium: It consists of layer of thin, flat, scale like cells with prominent nuclei. The main function is to provide the protection and safety to associated organs of the tissues and to help in the process of diffusion of the fluid material across the blood vessels and alveoli.

ii)Cuboidal Epithelium: It has cells which are polygonal in outline, but appear cuboidal in the vertical section. It lines small salivary and pancreatic ducts and thyroid vesicles. The cells take part in secretion, excretion and absorption. It provide mechanical support to organs, and in absorption area of organs.

iii)Columnar epithelium: It is characterized by presence of tall cell shaped polygonal column. The nucleus is located at the base of the cell. It covers the inner surface of intestine, stomach

and gallbladder. It is also found in the gastric and intestinal glands whose function are secretion or absorption.

iv)Ciliated Epithelium: There exists columnar or cubical cells in it and on whose free surfaces cilia is inner surfaces of some hollow organs like respiratory tract, fallopian tubes, bronchioles and small bronchi.

v)Pseudostratified Epithelium: It is made from the single layer of the columnar cells but it seems appear of two layers because some cells are smaller than others and nuclei are present at every layers. These usually found in Fallopian tubes and in upper respiratory tract. In longer cells celia exists.

vi)Glandular epithelium: Some columnar epithelium tissues are component of chemical substances and this tissues occurs in glands. Unicellular glands are present in intestine and mucous membrane. Multicellular glands composed of more than one gland cells. When secretion occurs and comes out through veins it is called Exocrine gland.

B)Compound Epithelim: These consists of more than one layer of cells. Being multilayers, they have little role in secretion or absorption but they provide protection to underlying tissues.

CONNECTIVE TISSUE: It provides structural framework and mechanical support to different tissues forming an organ. It also plays a key role in the body defence, tissue repair, fat storage and transmission of blood vessels to other tissues. Various types of connective tissues:

i)Areolar tissue: Areolar tissue exist in hollow inner part of the skin and on the arteries and veins. It connects various tissues and form cushions which helps in locating and confining the organs at their usual places and in maintaining their common original shapes. It contains fibroblast, histocytes, mast cells, plasma cells, leucocytes.

ii)Adipose tissue: In these cells the droplets of fat or lipid are to be filled up. In the body of the animals of cold countries such types of tissues are to be found in excess amount and that's why due to accumulation of such tissues the body of the animals is fatty.

iii)White Fibrous Tissue: Condensed white fibres are to be found which are parallel to each other. This tissue form the tendon which attaches muscles to the bone. Such tissues are extremely strong and partially elastic. White fibrous tissues provides locomotional motion between joints of skeleton of the skull.

iv)Yellow fibrous tissue: The fibres of such types of tissue is more thicker than the yellow fibres of areolar tissue. This tissue forms the ligament.

v)Tendons: It is extremely densed, powerful and fibrous connective tissue.

vi)Ligaments: It connects bones with another.

vii)Bone: This is solid, hard and powerful connective tissue. In the matrix of it, the epatite salts of calcium and phosphorous exist which provides stronger rigidity but complete lack of elasticity.

viii)Cartilage: The cartilage is connective tissue consisting of a dense matrix of collagen fibres and elastic fibres embedded in rubbery ground substance. The peak of the nose, exterior part of human ear etc are made of cartilage.

ix)**Blood**: This is fluid connective tissue whose cellular structure, composition and work is different. It contains two main components: Plasma and Blood Corpuscles. Plasma contains 55-60% of the blood. The plasma contains organic and inorganic substances and pale yellowishi color. Plasma contains water, protein, salts, glucose etc. The proteins of plasma are albumin, globulin, prothrombin, fibrinogen etc. These coexists in the form of colloids.

Blood corpuscles: The blood corpuscles are 40-45% of total blood and this part is called Haematocrit. These are 3 types RBC, WBC and platelets.

Red Blood Corpuscles: The human RBC lacks nucleus, mitochondria, golgibody, riosojmes. Male and Female contains 5 million & 4.5 million RBC in cmm. RBC contains Haemoglobin, is a fused protein in which a protein called globin and an iron ion are ound. OxyHaemoglobin carried 4 molecules of oxygen. The average life span of RBC is 120 days.

In fetus RBC formed from liver and spleen but in adulthood RBC form from red bone marrow. Vitamin B12, Folic acid and haemoglobin and iron are very important for production of RBC.

White Blood Cells: WBC does not have haemoglobin but nucleus is present. In human beings WBC is nearly 6000-9000 per cubic mm. Formation of WBC take place in bone marrow, spleen, lymph node. The average life span of WBC is 5-7 days. WBC is of two types Granulocytes, and Agranulocytes.

Granulocytes: Granulocytes have polyfied nucleus and of three types: Neutrophils, Eosinophils, Basofils.

Neutrophils: It contains 60-70% of total WBC. The main function of it is to destroy bacteria and other harmful organisms. It is also called Macrophages.

Eosinophilia: It contains 2-3% of total WBC. They enhance immunity and promote the anti allergic activities in human body.;

Basophils: They carry secreted substances like heparin, histamine, serotonin etc in the mast cells.

Agranulocytes: These are two types Lymphocytes and Monocytes.

Lymphocytes: These are tiny WBC whose nuclei are larger and spherical and its number is 20-28% of total WBC. It forms antibodies for immuning the human body.

Monocytes: These are larger size, Monocytes are 3-8% of total WBC. These also destroy bacteria and other harmful organisms.

PLATELETS: These cells absent nuclei and their structure are spherical. They present 0.15-0.45 million per cmm. The life span of platelets is nearly 7 days. They are worked in blood clot formation.

BLOOD GROUPS:

Blood Group	Antigen	Antibody	Give to	Receive from
A	A	B	A & AB	A & O
B	B	A	B & AB	B & O
AB	A & B	None	AB	AB, A, B & o
O	None	A & B	AB, A, B, O	O

MUSCULAR TISSUE: These tissues made of muscles fibres whose contractions and relaxations promote movement and locomotional activities. Muscular tissue is of three types: Smooth Muscle, Striped Muscle, Cardiac Muscle.

Smooth/Unstriped/Involuntary Muscle: The unstriped muscle cells are thin, longer, cylindrical shaped fibres which are arranged in a consistent, cohesive and in the form of a parallel branched bundle. These muscle contract and relax automatically. There is no self control on the wishes and action of living beings and that's why these are called involuntary muscles. Such tissues present at walls of stomach, intestine, ureter etc.

Striped/Voluntary/Skeletal Muscle: The cells of such tissues are longer, cylindrical and unbranched and on their outer parts light deep colored strips are ound, which are appeared in the alternative forms. There are larger number of nuclei which are present and confined towards the exterior and these muscles function according to the requirement and thus these are also called voluntary muscles.

Cardiac/Heart Muscles: It is present in Heart and it is involuntary. In the middle of every cell, one or two nuclei are found. All the compressions and relaxations through a consistent way take place by these tissues for all over the life.

NERVOUS TISSUE: The nerve tissue receives and transmits information and messages in the form of nerve impulses. This tissue is composed of Neurons and neuroglia cells. There are three main parts of the nerve tissue: Cyton, Dendron and Axon.

Cyton is main part of the nerve cell which nucleus and cytoplasm are found. In cytoplasm various proteineous and colored particles are found which are called Nissel Granules and which are folded aggregates of rough ER.

Dendron: The thin fibre passes through the cyton which is one or more is called Dendron.

Axon: A longer, thin nerve fibre which originates from cyton and which acts like a messenger from one neuron to another is called Axon. The axon forms intercommunicating junction, called synapses with dendrites and cell body or axon of some other neuron.

Nervous fibers are two types: Sensory/Afferent nerve fiber which carries impulses from receptor organs to brain or spinal cord. Motor/Efferent nerve fiber which carries impulses from brain to working organs.

CARDIOVASCULAR SYSTEM

The cardiovascular system is divided for descriptive purposes into two main parts: 1. The circulatory system, consisting of the heart, which acts as a pump, and the blood vessels through which the blood circulates. 2. The lymphatic system, consisting of lymph nodes and lymph vessels, through which colorless lymph flows.

The heart pumps blood into two anatomically separate systems of blood vessels: the pulmonary circulation, the systemic circulation.

The right side of the heart pumps blood to the lungs (the pulmonary circulation) where gas exchange occurs. The left side of the heart pumps blood into the systemic circulation, which supplies the rest of the body.

BLOOD VESSELS:

The heart pumps blood into vessels that vary in structure, size and function, and there are several types: arteries, arterioles, capillaries, venules and veins.

Arteries and arterioles: These are the blood vessels that transport blood away from the heart. They vary considerably in size and their walls consist of three layers of tissue. I) tunica adventitia or outer layer of fibrous tissue (II) tunica media or middle layer of smooth muscle and elastic tissue (III) tunica intima or inner lining of squamous epithelium called endothelium.

Veins and venules: The veins are the blood vessels that return blood at low pressure to the heart. The walls of the veins are thinner than those of arteries but have the same three layers of tissue. They are thinner because there is less muscle and elastic tissue in the tunica media. When cut, the veins collapse while the thicker-walled arteries remain open. Some veins possess valves, which prevent backflow of blood, ensuring that it flows towards the heart. Valves are abundant in the veins of the limbs, especially the lower limbs where blood must travel a considerable distance against gravity when the individual is standing.

HEART: The heart lies in the thoracic cavity in the mediastinum between the lungs. It lies obliquely, a little more to the left than the right, and presents a base above, andan apex below. The apex is about 9 cm to the left of the midline at the level of the 5th intercostal space, i.e. a little below the nipple and slightly nearer the midline. The base extends to the level of the 2nd rib. The heart is composed of three layers of tissue: pericardium, myocardium and endocardium.

Pericardium: The pericardium is made up of two sacs. The outer sac consists of fibrous tissue and the inner of a continuous double layer of serous membrane.

Myocardium: The myocardium is composed of specialised cardiac muscle found only in the heart. It is not under voluntary control but, like skeletal muscle, cross-stripes are seen.

Endocardium: This forms the lining of the myocardium and the heart valves. It is a thin, smooth, glistening membrane which permits smooth flow of blood inside the heart. It consists of flattened epithelial cells, continuous with the endothelium that lines the blood vessels.

Interior of the heart: The heart is divided into a right and left side by the septum, a partition consisting of myocardium covered by endocardium. After birth blood cannot cross the septum from one side to the other. Each side is divided by an atrioventricular valve into an upper chamber, the atrium, and a lower chamber, the ventricle. fibrous tissue. The right atrioventricular valve (tricuspid valve) has three flaps or cusps and the left atrioventricular valve (mitral valve) has two cusps.

The valves between the atria and ventricles open and close passively according to changes in pressure in the chambers. They open when the pressure in the atria is greater than that in the ventricles. During ventricular systole (contraction) the pressure in the ventricles rises above that in the atria and the valves snap shut preventing backward flow of blood. The valves are prevented from opening upwards into the atria by tendinous cords, called chordae tendineae, which extend from the inferior surface of the cusps to little projections of myocardium covered with endothelium, called papillary muscles.

Conducting system of the heart: The heart has an intrinsic system whereby the cardiac muscle is automatically stimulated to contract without the need for a nerve supply from the brain. There are small groups of specialised neuromuscular cells in the myocardium which initiate and conduct impulses causing coordinated and synchronised contraction of the heart muscle.

Sinoatrial node (SA node): This small mass of specialised cells is in the wall of the right atrium near the opening of the superior vena cava. The SA node is the 'pace-maker' of the heart because it normally initiates impulses more rapidly than other groups of neuromuscular cells.

Atrioventricular node (AV node): This small mass of neuromuscular tissue is situated in the wall of the atrial septum near the atrioventricular valves. Normally the AV node is stimulated by impulses that sweep over the atrial myocardium. However, it too is capable of initiating impulses that cause contraction but at a slower rate than the SA node.

Atrioventricular bundle (AV bundle or bundle of His): This is a mass of specialised fibres that originate from the AV node. The AV bundle crosses the fibrous ring that separates atria and ventricles then, at the upper end of the ventricular septum, it divides into right and left bundle branches. Within the ventricular myocardium the branches break up into fine fibres, called the Purkinje fibres. The AV bundle, bundle branches and Purkinje fibres convey electrical impulses from the AV node to the apex of the myocardium where the wave of ventricular contraction begins, then sweeps upwards and outwards, pumping blood into the pulmonary artery and the aorta.

The cardiac cycle: During each heartbeat, or cardiac cycle, the heart contracts and then relaxes. The period of contraction is called systole and that of relaxation, diastole. The normal number of cardiac cycles per minute ranges from 60 to 80. Taking 74 as an example each cycle lasts about 0.8 of a second and consists of: a) atrial systole — contraction of the atria (b) ventricular systole — contraction of the ventricles (c) complete cardiac diastole — relaxation of the atria and ventricles.

The superior vena cava and the inferior vena cava transport deoxygenated blood into the right atrium at the same time as the four pulmonary veins convey oxygenated blood into the left atrium. The atrioventricular valves are open and blood flows through to the ventricles. The SA node triggers a wave of contraction that spreads over the myocardium of both atria, emptying the atria and completing ventricular filling (atrial systole 0.1 s). When the wave of contraction reaches the AV node it is stimulated to emit an impulse which quickly spreads to the ventricular muscle via the AV bundle, the bundle branches and Purkinje fibres. This results in a wave of contraction which sweeps upwards from the apex of the heart and across the walls of both ventricles pumping the blood into the pulmonary artery and the aorta (ventricular systole 0.3

s). The high pressure generated during ventricular contraction is greater than that in the aorta and forces the atrioventricular valves to close, preventing backflow of blood into the atria.

After contraction of the ventricles there is complete cardiac diastole, a period of 0.4 seconds, when atria and ventricles are relaxed. During this time the myocardium recovers until it is able to contract again, and the atria refill in preparation for the next cycle.

Heart sounds: The individual is not usually conscious of his heartbeat, but if the ear or the diaphragm of a stethoscope is placed on the chest wall a little below the left nipple and slightly nearer the midline the heartbeat can be heard. Two sounds, separated by a short pause, can be clearly distinguished. They are described in words as 'lub dup'. The first sound, 'lub', is fairly loud and is due to the closure of the atrioventricular valves. This corresponds with ventricular systole. The second sound, 'dup', is softer and is due to the closure of the aortic and pulmonary valves. This corresponds with atrial systole.

PULSE: The pulse is a wave of distension and elongation felt in an artery wall due to the contraction of the left ventricle forcing about 60 to 80 millilitres of blood through the already full aorta and into the arterial system. When the aorta is distended, a wave passes along the walls of the arteries and can be felt at any point where a superficial artery can be pressed gently against a bone.

VITAMINS

Vitamins are two types: Water soluble vitamins, Fat soluble vitamins. Vitamin B and C are water soluble, while Vitamin A, D, E and K are fat soluble.

Vitamin	Diseases due to lack of vitamin	Presence
Vitamin A (Retinol)	Night Blindness, Xerophthalmia	Milk, egg, green vegetables, Cod Liver oil
Vitamin B1 (Thiamine)	Beri beri	Groundnut, liver, egg, pulses, sesamum
Vitamin B2 (Riboflavin)	Cracking in skin, red eyes, tongue etc	Liver, meat, green veg, milk
Vitamin B3 (Niacin)	Hair to be whitened, mental stupidity	Meat, groundnut, milk, tomato etc.
Vitamin B5 (Pantothenic acid)	Pellegra	Meat, leafy vegetables, potato, etc.
Vitamin B6 (Pyridoxine)	Anemia, skin disease	Liver, food grains, egg,
Vitamin B7 (Biotin)	Paralysis, body ache, hair fall	Meat, liver, egg, milk

Vitamin B12 (cyanocobalamin)	Pernicious anemia	Pulses, Liver, bean, vegetales,
Vitamin B9, Folic acid	Anemia, dysentery	Meat, liver, milk
Vitamin C	Scurvy, swelling of gems	Lemon, orange, tomato,
Vitamin D	Rickets, Osteomalacia	Fish liver oil, milk, egg, sun rays
Vitamin K	Delay in blood clotting	Green veg, tomato etc.

HUMAN SKELETAL SYSTEM

In the skeleton of the entire human body there exist 206 bones. In early childhood there are nearly 270 ones in emryogenic stage. But later some interconnected bones of the baby adjust and accommodate themselves in such a way that the number of bones are reduced to 206.

In human body the skeletal system has basically two parts: Axial skeleton and Appendicular skeleton.

Axial Skeleton: The skeleton which constructs main axis and central core o the human body is called Axial skeleton. The bones of the skull, vertebral column, chest etc come under this category. This skeleton consists of 80 Bones (29+26+1+24).

Head (29): The skull region of Head contains 8 bones, Facial bones contain 14, Bones of Ear 6, Hiden Part 1.

Backbone (Spinal Cord) (26): Neck contains 7, Chest contains 12, sacrum contains 1 and Tail 1.

Chest (25): Sternum 1 and Ribs 24.

Appendicular skeleton 126: Chest part contains Pectoral Girdle (4), Ankle Pelvic girld contains 2, Forelim Part contains 60, Hind limb part contains 60.

Name of Bones in particular Part of body:

Forelimb	Hindlimb	Skull	Facial
Humerus, Radius, Ulna, Carpals, Metacarpals, Phalanges	Femur, Tibia, Fibula, Patella, Tarsals, Metatarsals, Phalanges	Occipital,Parietal, Temporal, Frontal, Ethmoid, Sphenoid	Nigel, Turbinal, Lacrimal, Vomer, Zygomatic, Maxilla, Palatine, Mandible

TYPES OF JOINTS:

Ball and Socket Joint: Ex Pectoral girdle, Humerous Bone, femur & pelvic girdle.

Hinge joint: Ex Ankle, Elbow and Knee

Pivot Joint: First and second vertebrae of Neck, Joint of the Wrist (back and forth)

Gliding Joint: Joints of radius ulna & carpals, Zygapophyseal joint (facet joint)

Saddle Joint: Joint of carpals and metacarpals of the thumb.

Fixed Joint: Bones of Skull

DIGESTIVE SYSTEM

Organs of Digestive System: This is a long tube through which food passes. It commences at the mouth and terminates at the anus, and the various parts are given separate names, although structurally they are remarkably similar. The parts are: Mouth, Pharnyx, Oesophagus, Stomach, Small intestine, Large intestine, Rectum and anal canal.

Accessory organs: Various secretions are poured into the alimentary tract, some by glands in the lining membrane of the organs, e.g. gastric juice secreted by glands in the lining of the stomach, and some by glands situated outside the tract. The accessory organs are: 3 pairs of salivary glands, pancreas, liver and the biliary tract.

MOUTH: The oral cavity is lined throughout with mucous membrane, consisting of stratified squamous epithelium containing small mucus-secreting glands. The oral cavity is lined throughout with mucousmembrane, consisting of stratified squamous epithelium containing small mucus-secreting glands.

The part of the mouth between the gums (alveolar ridges) and the cheeks is the vestibule and the remainder of the cavity is the mouth proper. The mucous membrane lining of the cheeks and the lips is reflected on to the gums or alveolar ridges and is continuous with the skin of the face.

Tongue: The tongue is a voluntary muscular structure which occupies the floor of the mouth. It is attached by its base to the hyoid bone and by a fold of its mucous membrane covering, called the frenulum, to the floor of the mouth. The superior surface consists of stratified squamous epithelium, with numerous papillae (little projections), containing nerve endings of the sense of taste, sometimes called the taste buds. There are three varieties of papillae.

Vallate papillae, usually between 8 and 12 altogether, are arranged in an inverted V shape towards the base of the tongue. These are the largest of the papillae. Fungiform papillae are situated mainly at the tip and the edges of the tongue and are more numerous than the vallate papillae. Filiform papillae are the smallest of the three types. They are most numerous on the surface of the anterior two-thirds of the tongue.

Teeth: The teeth are embedded in the alveoli or sockets of the alveolar ridges of the mandible and the maxilla. Each individual has two sets, or dentitions, the temporary or deciduous teeth and the permanent teeth. There are 20 temporary teeth, 10 in each jaw. They begin to erupt when the child is about 6 months old, and should all be present after 24 months. Although the shapes of the different teeth vary, the structure is the same and consists of: the crown — the part which protrudes from the gum; the root — the part embedded in the bone; the neck — the slightly narrowed region where the crown merges with the root.

In the centre of the tooth is the pulp cavity containing blood vessels, lymph vessels and nerves, and surrounding this is a hard ivory-like substance called dentine. Outside the dentine of the crown is a thin layer of very hard substance, the enamel. The root of the tooth, on the other hand, is covered with a substance resembling bone, called cement, which fixes the tooth in its socket.

SALIVARY GLANDS: Salivary glands pour their secretions into the mouth. There are three pairs: the parotid glands, the submandibular glands and the sublingual glands.

Parotid Glands: These are situated one on each side of the face just below the external acoustic meatus. Each gland has a parotid duct opening into the mouth at the level of the second upper molar tooth.

Submandibular Glands: These lie one on each side of the face under the angle of the jaw. The two submandibular ducts open on the floor of the mouth, one on each side of the frenulum of the tongue.

Sublingual glands: These glands lie under the mucous membrane of the floor of the mouth in front of the submandibular glands.

Composition of saliva: Saliva is the combined secretions from the salivary glands and the small mucus-secreting glands of the lining of the oral cavity. About 1.5 litres of saliva is produced daily and it consists of: water, mineral salts, lysozymes, mucus, salivary amylase, immunogloulins etc. Salivary amylase that begins the breakdown of complex sugars, reducing them to the disaccharide maltose. The optimum pH for the action of salivary amylase is 6.8.

PHARYNX: The pharynx is divided for descriptive purpose into three parts, the nasopharynx, oropharynx and laryngopharynx. The nasopharynx is important in respiration. The oropharynx and laryngopharynx are passages common to both the respiratory and the digestive systems. Food passes from the oral cavity into the pharynx then to the oesophagus below, with which it is continuous. The walls of the pharynx are built of three layers of tissue.

OESOPHAGUS: The oesophagus is about 25 cm long and about 2 cm in diameter and lies in the median plane in the thorax in front of the vertebral column behind the trachea and the heart. It is continuous with the pharynx above and just below the diaphragm it joins the stomach. It passes between muscle fibres of the diaphragm behind the central tendon at the level of the 10th thoracic vertebra. The upper and lower ends of the oesophagus are closed by sphincter muscles. The upper cricopharyngeal sphincter prevents air passing into the oesophagus during inspiration and the aspiration of oesophageal contents. The cardiac or lower oesophageal sphincter prevents the reflux of acid gastric contents into the oesophagus.

STOMACH: The stomach is a J-shaped dilated portion of the alimentary tract situated in the epigastric, umbilical and left hypochondriac regions of the abdominal cavity. The stomach is continuous with the oesophagus at the cardiac sphincter and with the duodenum at the pyloric sphincter. It has two curvatures. The lesser curvature is short, lies on the posterior surface of the stomach and is the downwards continuation of the posterior wall of the oesophagus. Just before the pyloric sphincter it curves upwards to complete the J shape.

The stomach is divided into three regions: the fundus, the body and the antrum. At the distal end of the pyloric antrum is the pyloric sphincter, guarding the opening between the stomach and the duodenum. Stomach size varies with the volume of food it contains, which may be 1.5 litres or more in an adult. When a meal has been eaten the food accumulates in the stomach in layers, the last part of the meal remaining in the fundus for some time. Mixing with the gastric juice takes place gradually and it may be some time before the food is sufficiently acidified to stop the action of salivary amylase.

About 2 litres of gastric juice are secreted daily by special secretory glands in the mucosa. It consists of water, mineral salts, mucus secreted by goblet cells, HCl secreted by parietal cels, inactive enzyme precursors pepsinogen secreted by chief cells in the glands.

SMALL INTESTINE: The small intestine is continuous with the stomach at the pyloric sphincter and leads into the large intestine at the ileocaecal valve. It is a little over 5 metres long and lies in the abdominal cavity surrounded by the large intestine. In the small intestine the chemical digestion of food is completed and most of the absorption of nutrients takes place. The small intestine comprises three main sections. The duodenum is about 25 cm long and curves around the head of the pancreas. Secretions from the gall bladder and pancreas are released into the duodenum through a common structure, the hepatopancreatic ampulla, and the opening into the duodenum is guarded by the hepatopancreatic sphincter (of Oddi).

The jejunum is the middle section of the small intestine and is about 2 metres long. The ileum, or terminal section, is about 3 metres long and ends at the ileocaecal valve, which controls the flow of material from the ileum to the caecum, the first part of the large intestine, and prevents

regurgitation. The villi are tiny finger-like projections of the mucosal layer into the intestinal lumen, about 0.5 to 1 mm long. Their walls consist of columnar epithelial cells, or enterocytes, with tiny microvilli (1 μm long) on their free border. Goblet cells that secrete mucus are interspersed between the enterocytes. The pH of intestinal juice is usually between 7.8 and 8.0.

DIGESTION IN SMALL INTESTINE:

Pancreatic Juice: Pancreatic juice enters the duodenum at the hepatopancreatic ampulla and consists of: water, amylase, lipase, inactivated enzyme precursors trypsinogen, chymotrypsinogen, procarboxypeptidase. Pancreatic juice is alkaline (pH 8) because it contains significant quantities of bicarbonate ions, which are alkaline in solution. Trypsinogen and chymotrypsinogen are inactive enzyme precursors activated by enterokinase (enteropeptidase), an enzyme in the microvilli, which converts them into the active proteolytic enzymes trypsin and chymotrypsin. These enzymes convert polypeptides to tripeptides, dipeptides and amino acids. It is important that they are produced as inactive precursors and are activated only upon arrival in the duodenum, otherwise they would digest the pancreas. Pancreatic amylase converts al digestible polysaccharides not acted upon by salivary amylase to disaccharides.

Bile: Bile, secreted by the liver, is unable to enter the duodenum when the hepatopancreatic sphincter is closed; therefore it passes from the hepatic duct along the cystic duct to the gall bladder where it is stored. Bile has a pH of 8 and between 500 and 1000 ml are secreted daily. It consists of: Water, Bile salts, mineral salts, cholesterol. The bile salts, sodium taurocholate and sodium glycocholate, emulsify fats in the small intestine. The bile pigment, bilirubin, is a waste product of the breakdown of erythrocytes and is excreted in the bile rather than in the urine because of its low solubility in water. Bilirubin is altered by microbes in the large intestine.

Intestinal Secrections: The principal constituents of intestinal secretions are: water, mucus, mineral salts, enzyme enterokinase. Most of the digestive enzymes in the small intestine are contained in the enterocytes of the walls of the villi. Alkaline intestinal juice (pH 7.8 to 8.0) assists in raising the pH of the intestinal contents to between 6.5 and 7.5. Enterokinase activates pancreatic peptidases such as trypsin which convert some polypeptides to amino acids and some to smaller peptides. The final stage of breakdown to amino acids of all peptides occurs inside the enterocytes. Lipase completes the digestion of emulsified fats to fatty acids and glycerol partly in the intestine and partly in the enterocytes. Sucrase, maltase and lactase complete the digestion of carbohydrates by converting disaccharides such as sucrose, maltose and lactose to monosaccharides inside the enterocytes.

LARGE INTESTINE: This is about 1.5 metres long, beginning at the caecum in the right iliac fossa and terminating at the rectum and anal canal deep in the pelvis. Its lumen is larger than that of the small intestine. It forms an arch round the coiled-up small intestine. The colon is divided

into caecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum and anal canal.

The caecum is a dilated region which has a blind end inferiorly and is continuous with the ascending colon superiorly. Just below the junction of the two the ileocaecal valve opens from the ileum. The vermiform appendix is a fine tube, closed at one end, which leads from the caecum. It is usually about 13 cm long and has the same structure as the walls of the colon but contains more lymphoid tissue.

Ascending colon passes upwards from the caecum to the level of the liver where it curves acutely to the left at the hepatic flexure to become the transverse colon. The transverse colon is a loop of colon which extends across the abdominal cavity in front of the duodenum and the stomach to the area of the spleen where it forms the splenic flexure and curves acutely downwards to become the descending colon. The descending colon passes down the left side of the abdominal cavity then curves towards the midline. The sigmoid colon describes an S-shaped curve in the pelvis then continues downwards to become the rectum.

THE RECTUM: This is a slightly dilated section of the colon about 13 cm long. It leads from the sigmoid colon and terminates in the anal canal.

The anal canal: This is a short passage about 3.8 cm long in the adult and leads from the rectum to the exterior. Two sphincter muscles control the anus; the internal sphincter, consisting of smooth muscle fibres, is under the control of the autonomic nervous system and the external sphincter, formed by skeletal muscle, is under voluntary control.

PANCREAS: The pancreas is a pale grey gland weighing about 60 grams. It is about 12 to 15 cm long and is situated in the epigastric and left hypochondriac regions of the abdominal cavity. It consists of a broad head, a body and a narrow tail. The head lies in the curve of the duodenum, the body behind the stomach and the tail lies in front of the left kidney and just reaches the spleen. The abdominal aorta and the inferior vena cava lie behind the gland.

LIVER: The liver is the largest gland in the body, weighing between 1 and 2.3 kg. It is situated in the upper part of the abdominal cavity occupying the greater part of the right hypochondriac region, part of the epigastric region and extending into the left hypochondriac region.

The lobes of the liver are made up of tiny lobules just visible to the naked eye. These lobules are hexagonal in outline and are formed by cubical-shaped cells, the hepatocytes, arranged in pairs of columns radiating from a central vein. Between two pairs of columns of cells there are sinusoids (blood vessels with incomplete walls) containing a mixture of blood from the tiny branches of the portal vein and hepatic artery.

ENDOCRINE SYSTEM

The endocrine system is basically composed of various specific glands that produce and secrete hormones, chemical substances produced in the body to regulate the activity of cells or organs of the body.

Pituitary Gland: The pituitary gland located below the hypothalamus which infact lies exactly at mid point within the inner plane of palate and brain. The gland is called Master Gland. It also regulates the other endocrine glands and affects the nature, behavior, emotions, mood and reproductive activities. The following are hormones of Pituitary gland.

a)Somatotropic Hormone (STH): This hormone is respondent for growth and development of human body. It is called Growth Hormone. Excess secretion of STH is called Gigantism/Acromegaly. Lack of this hormone is called Dwarfism.

b)Thyroid Stimulating Hormone (TSH): This hormone activates thyroid gland to secrete thyroxine hormone.

c)Adreno Cortico Tropic Hormone (ACTH): It regulates the secretion activites of the adrenal cortex.

d)Gonadotropic Hormone (GTH): It is two types, which regulates working function of reproductive glands.

- Follicle Stimulating Hormone (FSH): This hormone helps in semen production of seminiferous tubules of the testes in men, and growth of follicle in the ovary of women.
- Luteinizing Hormone (LH): It activates interstitial cells of the body and secretes testosterone and estrogen.

e)Lactogenic Hormone: It helps to secret milk in the female for the babies. The hormone also activates the corpus luteum.

f)Antidiuretic Hormone (ADH): This hormone is made by hypothalamus and stored in the posterior pituitary gland. The ADH contracts the blood arteries and due to it the blood pressure of human body is enhanced. This hormone also useful in making a balance in the water level and osmotic pressure of body.

g)Melanocyte Stimulating Hormone (MSH): It effects on melanocytes (skin cels) which contain the black pigment called Melanin. MSH is produced by intermediate lobe of pituitary gland.

h)Oxytocin: Originates in hypothalamus and stored in posterior pituitary gland. It produces feeling of love and satisfaction and that’s why it is called Love Hormone. The release of oxytocin

causes the uterus to contract which causes laour contractions and tightens the uretus after a baby is born to delivery the placenta.

Thyroid Gland: It is butterfly shaped gland that lies in front of trachea just below the larynx. It releases thyroxine and triiodo thyronine hormones with use o Iodine. Lack of thyroxine causes Cretinism in children, myxoedema in adults. Lack of Iodine causes enlargement of thyroid gland is called simple goiter.

Parathyroid Gland: It is located in the throat (pharynx) just behind the thyroid gland. Two types of hormones are released: Parathyroid hormone (PTH) and Calcitonin. When calcium level is low PTH is released. When calcium is excessively increased in the blood then calcitonin hormone is secreted which is used in the controlling the amount of calcium in the blood of human body.

Adrenal Gland: It releases adrenaline and steroids like aldosterone and cortisal. These glands are located above the kidneys. Adrenaline hormone is called fight or flight hormone. When the adrenal glands are damaged and do not produce steroid hormones cortisol and aldosterone is called Addison's disease. It has two parts – exterior (Cortex) and Interior (Medulla).

Exterior part produces Glucocorticoids, Mineralocorticoids and sex hormones. Glucocorticoid (Cortisol) controls the metabolic activities of carbohydrates, protein and fat. Mineralocorticoid (Adlosterone) associated with re-absorption of Na and K salts through distal tubules of kidney.

Medulla part releases Adrenaline and Noradrenaline hormones.

Thymus Gland: Thymus gland is main organ of lymphatic system. Located in the upper chest region near the heart. The primary function of this gland is to promote the development of specific cells of the immune system called T-Lymphocytes or T-cells are white blood cells which protect against foreign organisms that have managed to infect the body cells.

Reproductive Glands (Gonad): The reproductive gland is also called gonad. The organs ovary and tested are sexual glands.

Ovary: It releases Estrogen, Progesterone and Relaxin. Estrogen promotes development & maintenance of female characteristics. Progesterone helps in breast growth and regulate condition of inner lining of the uterus. Relaxin produced by corpus luteum and it is directly respondent for the inhibition of uterine contraction. During the pregnancy relaxin is present in ovary and uterus through which the pubic symphysis is made soften and the uterine cervix becomes widen. Thus pelvic girdle becomes smooth and flattened which helps in child birth.

Testes: Testosterone is released by testes and it is naturally occurring androgen.

ADVERSE REACTIONS/Side Effects:

Barbiturates: intolerance, paroxysmal pain, depress foetal respiration, drug dependence (nystagmus, slurred speech, drug automatism, memory loss, megaloblastic anemia.

Drug automatism: If barbiturates are being employed as a hypnotic because of conusion and amnesia, patient may repeatedly take the barbiturate at night and poison himself. This phenomenon is called as drug automatism.

Hydantoin Derivatives: Skin rashes, drowsiness, vertigo, hyperplasia & hypertrophy of gums with edema and bleeding; hypertrichosis in children; cause fetal hydantoin syndrome when used in first termination of pregnancy.

Carbamazepine: Appear within first week of treatment includes giddiness, vomiting, mental confusion & skin rashe, diplopia and blurred vision; peripheral neuritis, obstructive jaundice.

Drug interactions of carbamazepine: induction of hepatic metabolism of oral contraceptive steroids, Vitamin D, theophylline, warfarin. Inhibition of carbamazepine metabolism by erythromycin, isoniazid, verapamil.

Sodium valproate: It increases appetite and may cause weight gain, dose related hair loss, hepatic damage, spina bifida is associated with its use during pregnancy.

Benzodiazepines: Drowsiness, lethargy, ataxia; dose related impairment of visual motor coordination, behavioral changes; may cause floppy baby syndrome in newborn when mother take before delivery.

Morphine: Dysphoria, constipation, mental clouding, vertigo, vomiting, increased pressure in biliary tract; respiration depression; hypotension, tolerance & drug dependence.

Pentazocine: sedation, sweating,hallucination, tolerance & physical dependence.

NSAID: Peptic ulceration, dyspepsia, gastrointestinal hemorrhage, hepatic damage on large doses, Reye's syndrome, neutropenia, thrombocytopenia, hemolysis, kidney damage.

- Phenylbutazone may reduce iodine intake may produce hypothyroidism, it also causes nephritis, exfoliative dermatitis, hepatitis.

Phenothiazine compounds (Antipsychotics): Intolerance, extrapyramidal effects (tremor,muscular rigidity, excessive salivation); blurring of vision, tachycardia, jaundice, long term use can cause gynecomastia, galactorrhea & menstrual irregularities.

Clozapine: Sedation, high incidence of grand mal seizure, agranulocytosis.

Olanzepine: Sedation, dry mouth, weight gain.

MAO Inhibitors: Headache, excitement, disturbed sleep, sedation, constipation, orthostatic hypotension. These drugs potentiates action of alcohol, amphetamine, ephedrine, anaesthetics, anticholinergics, barbiturates, Morphine, Pethidine.

Tricyclic Antidepressants: Allergic reaction like urticaria, skin rashes, pruritis, photosensitivity, dryness of mouth, difficulty in micturition, impotence, delayed ejaculation, tremors, muscle jerking, confusion, disorientation, cholestatic jaundice, agranulocytosis.

SSRI: Anxiety, insomnia, sexual dysfunction.

Lithium: Diarrhoea, vomiting, muscular weakness, cardiac arrhythmias, glycosuria, blurred vision, large doses cause cerebellar disturbances, epileptiorm seizures, hypotension; chronic administration causes hypothyroidism.

Levodopa: Vomiting, anorexia; depression with attempted suicide, agitation, confusion, hallucinations & delusions; postural hypotension, palpitation, some patients show positive coomb's test; urine is red colored.

Adrenaline* & *Noradrenaline: when given intravenously, sudden increase in BP, precipitating subarachnoid haemorrhage, may produce angina pain in persons with Ischemia Heart Disease.

Ephedrine: GI upset, insomnia, tremor, paranoid hallucinations.

Amphetamine: Anxiety, confusion, erratic behavior, visual hallucination, misperception, suicidal & homicidal tendencies, cardiac arrhythmia, death due to convulsion & coma; dependence.

Phenoxybenzamine: Miosis, dryness of mouth, nasal stuffiness & inhibition of ejaculation, palpitation, giddiness & postural hypotension.

Imidazoline Derivatives: Palpitation, flushing, apprehension, coldness, postual hypotension.

Beta Blockers: Beta blockers may cause sudden hypotension, bradycardia leading to cardiac asystole, non cardiac effects include nausea, vomiting, constiapation & bronchospasm. Prolonged used of propranolol cause fatigue, muscle cramps, lethargy & mental depression.

Cholinergic Drugs: flushing of face, sweating, salivation & lacrimation, hypotension and syncope, bronchial spasm.

Pilocarpine: As above, pulmonary edema in systemic therapy.

Cholinergic blocking drugs: Dryness of mouth, difficulty in swallowing, fever, constipation, blurring of vision, retention of urine in elderly.

Antihistamine: Sedation, fatigue, tinnitus, diplopia, drowsiness & impairment of coordination; dryness of mouth.

Methysergide: Vertigo, drowsiness, psychic disturbances, peripheral arterial insufficiency, precipitation of angina, aggravation of peptic ulcer, retroperitoneal fibrosis.

Cyproheptadine: Drowsiness, dizziness, ataxia, mental confusion.

Osmotic Diuretics: Headache, chills, polydipsia, pain in chest, rapid infusion of mannitol can cause cellular dehydration, pulmonary edema in patients with CHF.

Acetazolamide: metabolic acidosis, hypokalemia, rarely skin rashes.

Frusemide: Electrolyte and water disturbances, cardiac arrest following i.v. frusemide sudden death, hyperuricemia, very large doses can cause haring loss.

Spiranolactone: Drowsiness, decreased libido, gynecomastia & menstrual irregularity.

Sulphonamides: Allergy (skin rash, drug fever, eosinophilia); renal irritation, crystalluria, albuminuria in acidic urine; thrombocytopenia, agranulocytosis; kernicterus in foetus.

Nitrofurans: Rarely hemolytic anemia in G6PD deficiency patients, pulmonary infiltration & fibrosis, hepatitis; SLE like reaction. Polyneuritis is important adverse effects and deafness associated with tinnitus.

Nalidixic acid: Allergy (rash, pruritis, urticaria, photosensitivity), myalgia, convulsions.

Fluoroquinolones: Abdominal discomfort, diarrhea; confusion, nervousness, hallucination; rupture of shoulder, hand & Achilles tendons that require surgical repair, cartilage damage.

Penicillins: Allergy, anaphylactic shock, shows positive coomb's test.

Macrolides: Allergic reactions (eosinophilia, urticaria, dermatitis, lymphadenopathy); erythromycin may develop abdominal pain, they inhibit hepatic microsomal CyP450 enzymes.

Vancomycin: Local thrombophlebitis, generalized cutaneous reactions, impairment of eye, renal damage.

Bacitracin: Nephrotoxicity

Streptomycin: Allergy, damage to the 8^{th} nerve, impair vestibular functions, neuromuscular block & respiratory arrest, renal damage, azotemia.

Gentamicin: Photosensitivity, Vestibular damage, ototoxicity; azotemia.

Colistin: Acute renal failure, partial deafness, leucopenia, hepatotoxicity; transient disturabances of vision and speech.

Cephalosporin: Large doses can cause nephrotoxicity; kidney damage, hypoprothombinemia; platelet aggregation.

Carbapenems: GI Disturbances, allergic reactions can cause pseudomembranous colitis, no renal toxicity.

Tetracyclines: Anaphylactic shock; blood dyscrasias (aplastic anemia, leucopenia) rare; photosensitivity; brown/black coloration of nails, hepatis dysfunction & pancreatitis; renal impairment & azotemia; reversible fanconi like syndrome; tetracyclines chelated with calcium & deposited in bones & teeth, yellow coloration of teeth tookplace so avoid children below 12 years.

Chloramphenicol : Allergy, Bone marrow toxicity, Gray baby syndrome, peripheral neuritis.

Isonicotinic acid Hydrazide: Allergy, peripheral neuritis, burning & pain along sensory nerves; loss of memory and self control; muscle twitching, toxic encephalopathy; liver damage leads to death, epigastric distress.

Rifampicin: Skin rashes, eosinophilia, leucopenia; hepatic & renal failure.

Pyrazinamide: metallic taste, sulfurous eructation, mild skin rashes, rarely photosensitivity, rise in serum uric acid level.

Ethambutol: Optic neuritis, peripheral neuritis.

Ethionamide: skin rashes, alopecia; purpura, anaphylactic shock; GI irritation, gynecomastia, menorrhagia, pellagra like symptoms.

Cycloserine: Muscular weakness, slurred speech, convulsions, loss of judgement, hallucination.

Clofazimine: It imports reddish black color to skin; deposited in intestine which leads to diarrhea.

Quinine: Prutitus, angioneurotic edema, asthmatic attacks; black water fever (acute intravascular hemolysis, hemoglobinuria, fever), cardiac arrest, myocardial depressant; hypoglycemia.

Chloroquine: Large doses cause skin rashes, photosensitivity, pigmentation, blurring of vision/diplopia; insomnia, acute psychotic episodes.

Primaquine: Epigastric distress, abdominal distress, anemia & leucopenia; methaemoglobinemia, cyanosis, leucopenia.

FAMILY PLANNING

Hormonal Contraceptives:

a)Synthetic estrogens: Ethinylestradiol, Mestranol

b)Synthetic Progestagens:

- Pregnanes: Meegestrol, Medroxyprogesterone
- Estrogens: Norethisterone, Lynesterol
- Gonanes: Levonorgesterol

Hormonal contraceptives are used in two forms Oral Pi8lls & Depot Formulations.

Oral Pills: It prevents release of ovum from ovary by blocking pituitary secretion of gonadotropin. These are 3 types: Combined Pills, Minipill, Centchroman tablets.

Combined Pills: (30-35 mg of synthetic estrogen + 0.5-1 mg of progestogen). The pills is given orally for 21 consecutive days beginning on 5^{th} day of menstrual periods. It might be followed by one iron tablet.

Ex: Mala N – 1 mg of Norethisterone + 0.03 mg ethinylestradiol

Mala D – 0.5 mg D-Norgestrol + 0.03 mg ethinylestradiol.

Minipill: It contains progesterone only either norethisterone or levonorgestrel.

Centchroman Tablets: Ex Saheli.

Depot Formulation: It is sufficient for several months/years. These are:

Injectable contraceptives: 1 intramuscular injection of depot medroxy progesterone acetate (DMPA) is sufficient for 90 days.

Norethisterone Acetate: Intramuscular dose of 60 mg for every 60 days

PHARMACEUTICAL ANALYSIS

Definition:

It is a technique to identify and quantify any sample, compound or substance using

1) Manual Method
2) Chemical Method
3) Instrumental Method.

Types:

Pharmaceutical analysis can be classified into two types

1)Qualitative analysis

2)Quantitaive analysis.

Qualitative analysis determines purity of the sample, compound or any substance.

Quantitatve analysis determines the weight, length, quantity of particular compound.

Scope:

- Examination of Raw materials.
- Analysis of various drug samples.
- Qualitative and quantitative analysis of samples.
- Diagnosis of various disease by using chemical analysis.
- Determination of Radio active compounds.
- Determination of natural phytoconstituents.
- Determination of different sample of water.

Different techniques used in pharmaceutical analysis:

1) Instrumental analysis.

2) Non Instrumental analysis.

Non Instrumental methods	
➢ Biological methods • Invitro methods • Animal studies • Microbiological assays	➢ Chemical methods • Various chemical tests

Instrumental method:

1.Volumetric methods	**2.Spectral methods**	**3.Chromatography**	**4.Electro chemical methods**
1.Acid-Base -Non aqueous -Aqueous 2.Redox 3.Complexometry 4.Precipitation	1.Colourimetry 2.UV-Visible spectroscopy 3.NMR spectroscopy 4.Mass Spectroscopy 5.Spectro Fluorimetry	1.Planner chromatography -paper -TLC -HPTLC 2.Column Chromatography -HPLC -Size exclusion -Ion Exchange -Affinity chromatography -UPLC	1.Conductometry 2.coulometry 3.Potentiometry
	6.Other methods -DSC -TGA -RIA -ELISA		**5.Hyphenated techniques** 1.GC-MS 2.LC-MS 3.LC-NMR 4.GC-NMR 5.ICP-AAS 5.ICP-OES 6.ICP-MS

ERRORS: The Error is the nothing but the difference between the experimental mean value and a true value.

Errors can be expressed as either absolute error or relative error.

Absolute error=observed value-True value

Relative error=observed value – True value/True valueX100%

Types of errors:

Error	Reason
Methodic error	Slowness or incompleteness of chemical reactions, loss by volatility, adsorption of analyte on solid precipitate, instability of reagents, contaminants, chemical interferences.
Personal error	Caused due to person mistakes or carelessness of the analyst
Instrumental errors	Leakage in vacuum systems, Temperature fluctuations, calibration errors.

Method of expressing concentration:

1.Normality: No. of gram equivalent present per litre of solution and denoted by 'N'.

$$N=\frac{\text{No.of gram equivalent}}{\text{Vol. of solution (1litre)}}$$

$$\text{Gram equivalent}=\frac{\text{Molecular weight}}{\text{Acidity/Basicity}}$$

2.Molarity: No. of moles of solute present in one litre of solution and denoted by 'M'.

$$M=\frac{\text{No. of moles of solute}}{\text{Volume of solution(1litre)}}$$

3.Molality: No. of moles of solute present one kg of solvent and denoted by 'm'.

$$m=\frac{\text{No. of moles of the solute}}{\text{Mass of the solvent(in kg)}}$$

4.Formality: It is calculated based on the formula weight of the solute per litre of the the solution and denoted by 'F'.

$$F=\frac{\text{Formula weight}}{\text{Volume of soution}}$$

Percent concentration: Concentration is expressed in terms of

%W/W= weight of solute/weight of solutionx100

% V/V= Voume of solute/Volume of solutionx100

%W/V=Weight of solute/Volume of solutionx100

Parts per notation: Frequently used for very dilute concentration or for impurities.

1.Parts per million(ppm)

2.Parts per billion(ppb)

TITRATION

Diazotization: These are the titration used for estimation of drugs containing primary aromatic amino group.

Kjeldahl method : This Method is used to determine the nitrogen content in organic and inorganic samples.

Steps involved in kjeldahl method:

1.Digestion: The sample is digested in boiling concentrated sulphuric acid with the addition of a catalyst, until complete dissolution and oxidation. The nitrogen contained in the sample becomes Ammonium sulphate.

$$\text{Protein-(N)} + H_2SO_4 \xrightarrow{\text{catalyst}} (NH_4)_2SO_4 + CO_2 + H_2O$$

Catalyst is a combination of K_2SO_4(20g) ,Se powder (1g) and $CUSO_4.5H_2O$(1g).

This catalyst increased the boiling rate and rate of reaction.

2.Distillation: Adding an excess of sodium hydroxide solution , the ammonium ion is released in ammonia form , distilled and received on a boric acid solution or a sulphuric or hydrochloric acid.

$(NH_4)_2SO4 + 2NaOH \longrightarrow 2NH_3(gas) + Na_2SO_4+2H_2O$

3.Titration: The ammonia is determined with a volumetric acid solution or by back titration with sodium hydroxide solution of a known concentration. The results can be expressed in % N,%NH or protein (% N X factor).

Karl fischer Aquametry: This method is used to determine the moisture content or water content in any product or drug.

KFR reagent: This reagent is used as a titrant. Composition of this reagent contains 45g of iodine, 20g of sulphurdioxide, 80mg of pyridine and 400ml of methanol.

Note: Now a days pyridine is carcinogenic in nature i.e. why in place of pyridine we used to take imidazole.

Preparation:

400ml of methanol +80mg of pyridine

↓ Dissolve

Keep above solution in the freezing bath and supply sulphurdioxide in the cold solution till the weight increased by 20g.

↓

Add 45g of iodine and dissolve properly

↓ Kept for 24hrs

KFR is ready to use and 1ml of KFR is equal to 3.5mg of water

Step1: $H2O+SO2+I2 \longrightarrow SO3+HI$

Step2: $SO_3+C_5H_5N \longrightarrow C_5H_5N^+SO_2.O^-$

Step3: $C_5H_5N^+SO_2.O^-+CH_3OH \longrightarrow C_5H_5NHCH_3OSO_2O-$

Note: All the chemicals used in KFR is moisture free and presence of iodine will get to know the water content of drug.

Oxygen flask combustion method: It is a method used to identification and determination of halogens or sulphur produced by combusting organic compounds, which contain chlorine, bromine, iodine, fluorine or sulphur in a flask filled with oxygen.

Complexometry: This method is used to determine the metals by using complexing agents.

A complexing agents is an electron donating ion or molecule capable of forming one or more covalent or coordinate bonds with metal ions.

Complexing agents: EDTA, Dimethyl glyoxime, and salicylaldoxime are examples of complexing agents.

Indicators:

Indicator	Colour	Examples
1.Mordant black-II	Blue	Estimation of Ca, Mg, Zn, cd, Mn, Pb, and Hg.
2.Xylenol orange	Yellow in acid Red in alkaline	Aluminium sulphate, Aluminium hydroxide, Titanium dioxide, Zinc undecylenate.
3.Murexide	Violet	Ca
4.Calcon mixtures (or) solochrome dark		$CaCO_3$, $CaCl_2$

Masking and Demasking agents: Masking and Demasking agents are those which precipitate or complex ion selectively, inorder to estimate a specific ion.

Need of masking and demasking agents :

Ex. EDTA forms complexes with several metal ions during estimation of specific ion, other ionic impurities also estimated these gives incorrect results.

Sometimes when two or more ions are to be estimated in a mixture each ion has to be selectively titrated.

These can be done by one of the three method

1.Addition of Precipitants

2.Addition of Complexing agents

3.pH control

1.Addition of precipitants:

Interfering ions	Precipitants
Copper, cobalt, Lead	Sodium sulfide, Thioacetamide
Lead, Barium	Sulphate
Lead, calcium	oxalate
Lead, calcium, Magnesium	Flouride
Zinc, copper	Ferrocyanide
Many heavy metals	Cupferron, 8-Hydroxy quinoline

Addition of Complexing agents:

Interfering ions	Complexing agents
Aluminium, Iron, Titanium	Ammonium fluoride
Ferric	Ascorbic acid+ Ferrocyanide
Mercury, cadmium, zinc, Arsenic, Antimony, Tin, Lead, Bismuth	Dimercaprol in alkaline medium
Mercury	Potassium Iodide
Aluminium, Titanium	Titron
Aluminium, Iron	Triethanolamine
Silver, Copper, Mercury, Iron, Zinc, Cadmium, Cobalt, Nickel	Potassium cyanide in alkaline medium

Non aqueous titration:

Non-aqueous titrations are those in which the titration of weakly acidic or basic substances are carried using Non-aqueous solvents.

Types of solvents:

1)Aprotic solvents

2)Protogenic solvents

3)Protophillic solvents

4)Amphiprotic solvents

Solvents	Conditions	Examples
1.Aprotic solvents	▪ Chemically inert ▪ Low dielectric constant ▪ Do not favour Ionisation	Ex: Chloroform, Benzene
2.Protogenic solvents	▪ Genic- Producing ▪ Acidic substance	Ex:H_2SO_4, HCl,HNO_3
3.Protophillic solvents	▪ Phillic-loving ▪ Basic Substances ▪ Forms solvated protons	Ex:$HClO_4$ in CH_3COOH
4.Amphiprotic solvents	▪ Both protogenic and protophillic properities	Ex:Water, acetic acid, alcohol

Indicator:

Indicator	Colour change		
	Basic	Neutral	Acidic
Crystal violet	violet	Blue-green	Yellowish-green
α-Naphtholbenzein	Blue or blue-	Orange	Dark-green

	green		
Oracet blue B	blue	purple	pink
Quanildine Red	magneta	_	Almost colourless

Potentiometry: It is an elctroanalytical method which is used to find the concentration of a solute in solution.

Nernst equation:

$$E = \overset{\circ}{E} + \frac{2.303RT}{nF} Log \frac{(Product)}{(Reactant)}$$

Where, E = Potential of electrode or cell

$\overset{\circ}{E}$= Standard potential of electrode or cell

R = $8.314JK^{-1}mol^{-1}$

F = 96500 C/mole

At 25°c, 2.303/F= $0.0592Vmole^{-}$

$$E = \overset{\circ}{E} + \frac{0.0592}{n} Log \frac{(Product)}{(Reactant)}$$

Reference electrode: These are the standard electrodes which is stable in the solution of potential.

Ex: Hydrogen Electrode, Saturated calomel electrode, Silver-silver chloride electrode

Indicator electrode: Indicator electrode indicates the potential or pH of a solution.

Ex: Hydrogen electrode, Antimony-Antimony oxide electrode, Glass electrode.

Potentiometric titrations:

These are the titrations in which the end point of titrations can be determined by measuring the potential or changes in the potential of a solution caused by the addition of titrant.

Titrations can be done manually or under automation. When it is done manually, a beaker with a stirrer and a pipette are sufficient .

Applications:

The following types of titration can be done by potentiometric method

- Acid- Base titration
- Redox titration
- Diazotisation titration
- Complexometric titration
- Dead stop end point technique

Type of titration	Electrodes used	Titrate Vs Titrant
1.Acid-Base • Aqueous medium • Non aqueous medium	Indicator electrode :Glass electrode Reference electrode: Saturated calomel electrode	1.CH3COOH Vs NH4OH 2.CH3COOH Vs NaOH 3.HCl Vs NH4OH 4.HCl Vs NaOH Ex: Barbituric acid Vs LiOMe
• Redox titration	Reference electrode: Saturated calomel electrode Indicator electrode: platinum wire or foil	Ex: Ferrous sulphate Vs KMnO4 Sodium Arsenite Vs KBrO3
• Diazotisation titration	R.E: SCE I.E: Glass electrode	Ex: Alkaloid, Amine, Sulpha Drugs which contain aromatic primary amino group Vs 0.1N sodium nitrite
• Precipitation titration	R.E :SCE I.E : Silver wire electrode	Determination of mercury, silver, lead, copper to form insoluble salts

Conductometry:

Conductometry is the measurement of conductivity of a solution due to the mobility of cations and anions towards respective electrode.

Specific Conductance : It is the conductance offered by a substance of 1cm length and 1Sq.cm Surface area and units are mhos cm^{-1}.

Equivalent conductivity : It is the conductivity of a solution containing equivalent weight of the solute between electrodes 1cm apart and 1sq.cm surface area and units are $mhoscm^{-1}$.

Equivalent conductivity: Specific conductivity (Kv) X Volume (cc) of solution containing 1g equivalent weight of electrolyte.

Conuctometric titrations:

Titration	Principle
A. Acid-Base Titrations • Strong acid Vs Strong base	HCl Vs NaOH ▪ The first part of the curve shows steep fall in conductivity because of decrease in H^+ and the second part of the curve shows gradual increase because of increase in OH^-.
• Strong acid Vs Weak base	HCl Vs NH_4OH ▪ The first part of the curve shows steep fall in conductivity because of decrease in H^+ and second part of the curve shows a plateau.
• Weak acid Vs Strong base	CH_3COOH Vs NaOH ▪ The first of the curve shows a gradual increase and second part of the curve shows steep increase because of increase in OH^-.
B. Precipitation titration	KCl Vs $AgNO_3$ ▪ The part of the curve shows no increase in conductivity as there is only replacement of chloride ions with nitrate ions and the second part of the curve increases because of increase in the concentration of silver as well as nitrate ions.

Polarography:

Polarography is the study of solution or of electrode processes by means of electrolysis with two electrodes.

Half wave potential : This is the potential at point of inflection in the current –voltage curve. $E^{1/2}$ is characteristic or specific for every electroreducible ion or functional group . At this potential , 50% of the reduced form and 50% of the oxidized form are present . The obtained $E^{1/2}$ value for

a compound is compared with the standard values and the substance can be identified. Thus Half wave potential is the qualitative aspect which serves to identify a substance.

Different currents used in polarography:

Currents	Principle
1.Residual current (i_r)	It is the combination of relatively larger condenser current and very small faradic current . Condensor current is due to the formation of Helmholtz double layer at the mercury surface and faradic current is due to the traces of impurities.
2.Migration current(i_m)	It is due to migration of cations from the bulk of the solution towards cathode due to diffusive force, irrespective of concentrative gradient. This depends on the proportion of the analyte of interest. To eliminate the migration current, a large proportion of supporting electrolyte (KCl).
3. Diffusion current (i_d)	It is due to the actual diffusion of electroreducible ion from the bulk of the sample to the surface of the mercury droplet due to concentration gradient . Current carried by such ions under such conditions is called as diffusion current.
4.Limiting current(i_l)	The current reaches a steady value called as the limiting current .the rate of diffusion of ions is equal to the rate of reduction and the state of electrode is said to be concentration polarized.

Ilkovic equation : The diffusion current at its limiting value DME is given by Ilkovic equation as follows.

$$i_d = 607\ n\ C\ D^{1/2}\ m^{2/3}\ t^{1/6}$$

Where i_d = diffusion current due to electroreducible ions

n= no.of electrons involed in the reduction of one molecule

C= conc. expressed in mmol/lit

D= Diffusion coefficient of ions (cm^2/sec)

m= Wt of mercury flowing through capillary (mg/sec)

t= drop time in seconds (2 to 7 seconds)

Dropping mercury electrode (DME):

It is a polarisable electrode and a gradually increasing negative potential can be applied. DME consist of a fine capillary with a bore size of 20-50µ and is connected to a mercury reservoir . By adjusting the height of the reservoir the drop time can be adjusted . Drop time is the time taken for every fresh droplet of mercury formed from the capillary. It is useful ove the range of +0.4 to -1.8V.

Amperometric titration:

The potential applied between polarisable and non-polarisable electrode is kept constant and the diffusion current is measured during the titration.

Rotating platinum electrode: It consist of a glass rod with a bent platinum wire at its tip and rotates at about 600rpm. Wire contacts are made through a mercury reservoir at the top so that potential can be applied and the current is measured .

Types of amperometric titrations:

Compound	Principle
1.Electro reducible Vs Non reducible ion	• Lead Vs sulphate ions The first part of the curve shows a decrease in current due to decrease in the concentration of lead ions in solution and this is due to precipitation as lead sulphate by sulphate ions .At the end point as all the lead ions are reacted, the diffusion current value reaches a minimum. The addition of sulphate ions after the end point does not cause change in diffusion current , as it is non reducible ion.
2. Non reducible Vs Electro reducible	• Chloride Vs Silver ions As the chloride ions are non reducible ions so the diffusion current does not cause any change. The addition of silver ions also does not cause any change in diffusion as the silver chloride precipitate formed. After the end point the addition of silver ions causes steady increase in diffusion current .

3.Electroreducible Vs Electroreducible ions	• Lead Vs Dichromate ions The first part of the curve shows steep decrease in diffusion current due to decrease in the concentration of lead ions and all the lead ions reacted and are precipitated as Lead chromate. After the end point the addition of dichromate ions cause in increase in diffusion current.

Chromatography:

Chromatography is the separation of a mixture into individual components using a stationary phase and a mobile phase.

Theory of chromatography :

- ✓ Adsorption chromatography
- ✓ Partition Chromatography

1. Adsorption chromatography:

Stationary phase: Solid

Mobile phase : Liquid

The compound which has more affinity towards stationary phase travels slower and the compound which has lesser affinity towards stationary phase travels faster. Hence the compounds are separated. No two compounds have the same affinity for a combination of a stationary phase, mobile phase and other conditions.

Ex: Gas-Solid chromatography, Thin layer chromatography, Column chromatography, and HPLC.

2. Partition chromatography:

Stationary phase: Liquid coating
Mobile phase : Liquid

When a mixture of compounds are dissolved in the mobile phase and passed through a column of liquid stationary phase, the component which is more soluble in the mobile phase travels faster and the component which is more soluble in stationary phase travels slower. Thus the components are separated because of the differences in their partition coefficients.

Ex: Gas- Liquid chromatography, Paper Partition chromatography, Column Partition chromatography.

Based on the modes of chromatography: Two types and they are based upon the polarity of the stationary phase and mobile phase.

Normal phase: Stationary phase-Polar

Mobile phase -Non-polar

Reverse phase: Stationary phase-Nonpolar

Mobile phase -Polar

Plate theory: A theoretical plate is an imaginary or hypothetical unit of a column where distribution of solute between stationary phase and mobile phase has attained equilibrium.

HETP - Height Equivalent to a Theoretical Plate:

A theoretical plate can be of any height, which decides the efficiency of separation. If HETP is less, the column is more efficient . If HETP is more , the column is less efficient.

$$HETP = \frac{length\ of\ the\ column}{\text{no.of theoritical plates}}$$

HETP is given by the **Van Deemeter equation**

$$\text{HETP} = A + \frac{B}{u} + Cu$$

Where A= Eddy diffusion term

B= Longitudinal diffusion term which depends on flow rate

C= Effect of mass transfer which depends on flow rate

u= Flow rate or velocity of the mobile phase

Efficiency: Efficiency of a column is expressed by the number of theoretical plates. It can be determined by using

$$n = 16\frac{Rt2}{W2}$$

Where n= no. of theoretical plates

Rt= retention time

w= Peak width at base

If the number of theoretical plates is high, the column is highly efficient. If the number of theoretical plates is low, the column is less efficient.

Paper chromatography:

This is the technique in which the analysis of unknown substances is carried out mainly by the flow of solvents on specially designed filter paper.

Types : 1. Paper adsorption chromatography

S.P= Silica paper

M.P= Solvent

2. Paper Partition chromatography:

S.P= Moisture cellulose fibres present in filter paper

M.P= Solvent

Principle: The main principle is partition

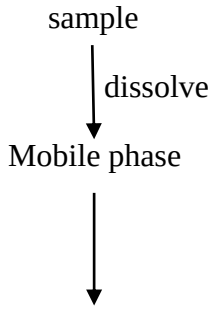
S.P= Cellulose layer in filter paper contains moisture

M.P= Organic solvents or buffer

Requirements:

- Stationary phase and papers used
- Application of sample
- Mobile phase
- Development technique
- Detecting or visualizing agents

- ✓ Stationary phase and papers used: Whatman filter papers of different grade like NO.1, NO.2, NO.3, NO.3MM, NO.4, NO.17, NO.20
  Papers differ in size, shapes, porosities and thickness.
  Choice of filter paper depends on thickness flow rate, purity.
- ✓ Sample application:



Applied through capillary tube

- ✓ Mobile phase: Pure solvents, buffer solution are used. Some of them are

1.Hydrophillic Mobile phase:

Isopropanol:Ammonia:Water-9:1:2

n-Butanol:glacial acetic acid:water-4:1:5

Methanol:Water-3:1

t-Butanol:Water:Formic acid -40:20:5

2.Hydrophobic mobile phase:

Kerosene: 70% Isopropanol

Dimethyl ether :Cyclohexane

- ✓ Development technique :

Technique	procedure
1.Ascending development	The spot are kept at bottom portion of the paper and kept in a chamber with mobile phase at the bottom, the solvent flows against gravity.
2.Descending development	This is carried out in a special chamber where the solvent holder is at the top. The spot is kept at the top and the solvents flows from down the paper and development is faster.

3.Ascending-Descending development	This is a combination of two techniques. Only the length of separation is increased by using this technique.
4.Circular/radial development	The spot is kept at the centre of a circular paper.The solvent flows through a wick at the centre and spreads in all directions uniformly. The individual spots looks alike concentric circles after development
5.Two dimensional development	This technique is similar to 2- dimensional TLC. The paper is developed in one direction and after development , the paper is developed in second direction allowing more compounds or complex mixturesare separated into individual spots.

- ✓ Applicatons:
    1. Identification of drugs

Drug	Mobile Phase	Detecting agent
Erythromycin estolate	Isobutyl methyl ketone	Nutrient agar containing Bacillus pumilus
Gentamycin	Chloroform: Methanol: Ammonia: water(10:5:3:2)	Ninhydrin in pyridine acetone mixture
vancomycin	t-Amyl alcohol: Acetone: Water(2:12)	Nutrient agar containing Bacillus subtillis

2.Identification of impurities

Drug	Mobile phase	Detecting agent
Hydroxocobalamin	s-Butyl alcohol: acetic acid: Potassium cyanide	Elution and measurement of absorbance at 361nm

3. Separation of carbohydrates, vitamins, antibiotics, proteins, alkaloids, glycosides, amino acids
4. Identification of foreign substances in drugs
5. Analysis of metabolites of drugs in blood and urine.

Thin layer chromatography:

The components are separated on a thin layer chromatographic plate based on the affinity of the components towards the stationary phase.

- It is a simple rapid technique
- Efficiency of separation:
  Very small particle size increase the particle size
- Need less solvent and stationary phase

Stationary phase:

Name	Composition	Adsorbent: Water ratio
Silica gel H	Silicagel without binder	1:1.5
Silica gel G	Silicagel + $CaSO_4$	1:2
Silicagel GF	Silicagel + Binder + flourescent indicator	1:2
Cellulose powder	Cellulose without binder	1:5
Polyamide powder	Polyamide	1:9

Glass plates:

Glass plates have specific dimensions like 20cm X 20cm, 20cm X 10cm, 20cmX5cm.

Preparation and activation of TLC plates:

Name of the preparation	Procedure
Pouring	The slurry is prepared and poured on the glass plate which is maintained on a leveled surface and the slurry is spread uniformly on the surface of the glass plate. After setting the plates are dried in an oven.
Dipping	Two plates are dipped in to the slurry and are separated after removing from the slurry and later dried.
Spraying	The slurry is sprayed on a glass plate using a sprayer .Uniformity is not maintained all over the plate.
Spreading	The glass plates of specific dimension are stacked on the base plate. The slurry after preparation is poured inside the reservoir of TLC spreader. The thickness of the adsorbent layer is adjusted by using knob in the spreader . Normally a thickness of 0.25mm is used for analytical purpose ad 2mm thickness for preparative purpose. The spreader is rolled only once on the plates. This is done to avoid cracks on the surface of adsorbent. After setting the plates are activated by keeping in an oven at 100°C to 120°C for 1 hour.

Application of sample: 2-5 µl of a 1% solution of either standard or sample is spotted using a capillary tube or micropipette. The spots should kept atleast 2cm above the base of the plate and the spotting area should not be immersed in the mobile phase in the development tank.

Mobile phase:

Petroleum ether, Carbon tetrachloride, Cyclohexane, Carbondisulfide, Ether, Acetone, Benzene, Toulene, Ethyl acetate, Chloroform, Alcohols, Water, Pyridine, Organic acids etc.

Compositions are done by trial and error method.

Development technique:

1. One dimensional development
2. Two dimensional development
3. Horizontal development
4. Multiple development

Applications:

1. Separation of mixture of drugs of chemical or biological origin, plants and extracts etc.
2. Separation of carbohydrates, vitamins, antibiotics, proteins, alkaloids, glycosides etc
3. Identification of drugs:

Drug	Stationary phase	Mobile phase	Detecting agent
Aminocaproic acid	Silica Gel G	Alcohol:H_2O:NH_3	Ninhydrin in alcohol and pyridine
Amoxycillin trihydrate	Silica Gel H.G-254	Buffer pH 6: acetone (4:1)	NaOH + starch + glacial acetic acid + Iodine in potassium iodide
Ampicillin for oral suspension	Cellulose M.N-300	Citric acid : Butyl alcohol(5:1)	Starch iodide reagent
Chlorpromazine HCl	Silica Gel G	Ether: Ethyl acetate: NH_3	UV 254nm
Levodopa	Micro crystalline cellulose	n-Butanol: Glacial acetic acid: Water(50:25:25)	Potassium ferricyanide

Column chromatography:

Based on the nature of stationary phase , i.e. whether it solid or liquid, it is called as column adsorption chromatography or column partition chromatography. When a mixture of components is dissolved in the mobile phase is introduced into the column , the individual components move with different rates depending upon the relative affinities. The compound with lesser affinity towards the stationary phase (adsorbent) moves faster and hence it is eluted out of

the column and the compound with greater affinity towards the stationary phase moves slower down the column and eluted later.

Requirements:

1. Stationary phase: It should have high mechanical stability.

It should be inert and should not react react with solute or other solvent.

Ex: Activated Mg Silicate, Activated alumina, Activated charcoal, Activated Magnesia, Calcium carbonate, Calcium phosphate, Magnesium oxide, Sucrose, Starch, Inulin, Talc.

Selection of stationary phase depends upon

1. Removal of impurities
2. No. of components to be separated
3. Affinity differences between components
4. Length of the column used
5. Quantity of absorbent used

2. Mobile Phase :

To introduce the mixture into the column – As solvent

To develop the zones for separation –As developing agent

To remove pure component out of the column- As eluent

Ex: Petroleum, ether, Carbon tetrachloride, Cyclohexane, Acetone, Benzene, Toulene, Esters, Chloroform, water, Pyridine, Organic acids etc

3.Column characteristics: The material of the column is mostly good quality neutral glass. It should not be affected by solvents, acids or alkalies. For more efficiency the ratio of length and diameter can be 100:1.

4. Preparation of the column: The bottom portion of the column is packed with cotton wool or asbestos pad.

i. Dry packing technique

ii. Wet packing technique

5.Introduction of sample: The entire sample is introduced into the column at once and gets

adsorbed on the top portion of the column.

6.Development technique: After the introduction of the sample, by elution techniques, the individual components are separated out from the column. The two techniques are:

i. Isocratic elution : Same solvent composition or solvent of same polarity is used throughout the process of separation.

ii. Gradient elution: Solvent of gradually increasing polarity or increasing elution strength are used during the process of separation.

Applications:

1. These can be used for the separation of several classes of drugs like alkaloids, glycosides, amino acid, plant extracts, drugs and formulations etc

2. Removal of impurities of purification process

3. Isolation of active constituents

4.Isolation of metabolites from biological fluids

5. Estimation of drugs or crude drugs

HPLC: High performance liquid chromatography

Instrumental requirements:

Components	Procedure
1. Pumps	The solvents or mobile phase used must be passed through the column at high pressure at about 1000 to 3000psi. Mechanical pumps operate with constant flow and uses a sapphire piston. Pneumatic pumps operate with constant pressure and use highly compressed gas Check valves are used to control the flow rate of solvent and back pressure .
2. Mixing unit	Pulse dampners are used to dampen the pulses observed from the way baseline caused by the pumps. Mixing unit is used to mix solvents in different proportions and pass through the column.
3. Solvent degassing	a. Vaccum filtration: This can be remove the air bubbles b. Helium purging: This is by passing helium through the solvent c. Ultrasonication : which converts ultra high frequency to mechanical vibrations and removal of air bubbles.

4. Injector	a. Septum injectors- The sample through a rubber septum and the septum has to withstand high pressure. b. Stop flow- The flow of mobile phase is stopped for a while and the sample is injected through a valve. c. Rheodyne injector- Most popular injector and has a fixed volume loop like 20µl or 50µl Injector has two modes i.e, load position and inject mode.
5. Analytical column	a. Column material: Stainless steel, glass, and Polyethylene b. Column length: varies from 5cm to 30cm c. Column diameter: Ranges from 2mm to 50mm d. Particle size: From 1µ to 20µ. e. Particle nature: Spherical, uniform sized , porous materials are used.
6. Detectors	UV detector : Based on the light absorption of sample. i. Fixed wavelength ii. Variable wavelength Flourimetric detector is based on the fluorescent radiation emitted and the Vs Time Vs wavelength. Conductometric detector : Based upon electrical conductivity, the response is recorded when the sample has conducting ions like anions and cations. Photo diode array detector : Radiation of all wavelength fall on the detector and the resulting spectra is a three dimensional plot of Response Vs Time Vs Wavelength.

Applications:

1. It is used in the qualitative analysis.
2. It is used to check the purity of a compound.
3. It is used to check impurities
4. It is used to identification of a compound

Gas chromatography:

Stationary phase : Solid or liquid

Mobile phase: Gas

Principle : The principle of separation in GLC is partition. Gas is used as mobile phase and liquid is coated on a solid support is used as stationary phase. Components are separated according to their partition coefficient.

Two criteria : 1. Volatility

2.Thermostability

Requirements:

Components	Principle
1. Carrier gas	Hydrogen : Better thermal conductivity Low density a. Helium : Excellent thermal conductivity Expensive Good carrier gas b. Nitrogen: Inexpensive Carrier gas should be inertness, high purity, Easily available, cheap, less risk of explosion.
2. Injection Devices	Silicon rubber
3.Column	Glass or stainless steel

Spectral methods: These are the method use light absorption or emission characteristics of drugs.

Ultraviolet spectroscopy: It is the study of UV radiation which ranges from 200nm to 400nm

Principle: Any molecule has either n, π or σ or a combination of these electrons. These bonding (σ & π) and non-bonding (n) electrons absorbs the characteristic radiation and undergoes transition from ground state to excited state.

Types of electronic transitions:

Transition	Principle
1. $n \rightarrow \pi^*$	These transition requires lowest energy(longer wavelength). The peaks due to this transitions is called R-bands. These can be seen in compounds where 'n' electrons is present in a compound containing double bond or triple bond Eg: Aldehydes or ketones, nitrocompounds etc
2. $\pi \rightarrow \pi^*$	These energy requirement of transition is between $n \rightarrow \sigma^*$ and $n \rightarrow \pi^*$. But extended conjugation and alkyl substituents shifts the λ_{max} towards longer λ(Bathochromic shift). Extended conjugation shifts λ_{max} to such an extent that the λ_{max} falls in the colorimetric region eg: plant pigments like β-carotene, lycopene.
3. $n \rightarrow \sigma^*$	This transition occurs in saturated compounds, with hetero atom like S, O, N or Halogens. It requires lesser nergy when compared to $\sigma \rightarrow \sigma^*$ transition.Normally the peaks due to this transitionoccurs from 180nm to 250nm.
4. $\sigma \rightarrow \sigma^*$	Of all the electronc transitions, this type of transition requires higher energy. This is observed with saturated compounds and the peaks do not appear in UV region I.e. 125-135nm.

Instrumentation:

Components	Working principle

1. Source	a. Hydrogen discharge lamp: More stable, robust and widely used , radiation ranges from 120-350nm , it consist of hydrogen under high pressure. b. Deuterium lamp: It is filled with deuterium and expensive c. Xenon arc lamp: Xenon at 10-30 atmospheric pressure is filled in and has two tungsten electrodes and intensity is greater than hydrogen discharge lamp. d. Mercury lamp: contains mercury vapour and offers bands which are sharp and it is not widely used.
2. Monochromators	Grating monochromators are used, Filters and prism monochromators are not used because of low resolution
3. Sample cells	Sample cell made up of Quartz and the pathlength of the cells are 10mm or 1cm
4. Solvents	Solvents for a sample is selected in such a way that the solvent neither absorbs in the region of measurement nor affects the absorption of the sample. Some common solvents used and their asorption regions are Water-191nm Cyclohexane-195nm Methanol-203nm Ethanol-204nm Ether -215nm Chloroform-237nm
5.Detector	Photomultiplier tube

Applications:

1. It is used to detect the impurities present in the drug
2. It is used to detect the structure elucidation of organic compounds
3. It is used to perform simultaneous estimation method of compounds
4. It is used in the determination of molecular weight

5. It is used in the determination of dissociation constant of acids and bases.

6. It is used in the quantitative analysis of Pharmaceutical substances:

Drug	Solvent	Wavelength(nm)	$E_{1cm}^{1\%}$
Acetazolamide	0.1N HCl	265	474
Allopurinol tablets	0.1N HCl	250	563
Bisacodyl tablets	$CHCl_3$	264	148
Carbamazepine tablets	Alcohol	285	490
Chloramphenicol capsules	water	278	288
Chlorpheniramine maleate tablets	0.5N H_2SO_4	262	147

Flourimetry:

Principle: Absorption of UV/Visible radiation causes transition from singlet ground state to singlet excited state. As this excited state is not stable, it emits the excess energy and returns back to ground state.

Electronic states :

1. Singlet ground state : A state in which all the electrons in a molecule are paired ↓↑
2. Doublet state: A state in which an unpaired electron is present eg: free radical ↓ or ↑
3. Triplet state: A state in which unpaired electrons of same spin ↑ ↑
4. Singlet excited state: A state in which electrons are unpaired but of opposite spin like ↑ ↓

Flourescence: It is the phenomena of emission of radiation when there is transition from singlet excited state to singlet ground state. The wavelength of absorbed radiation is called excitation wavelength and that of emitted radiation is called as emission wavelength.

Phosphorescence: At favourable conditions like low temperature and absence of oxygen , there is transition from excited singlet state to triplet state which is called inter system crossing. The emission of radiation when electrons undergo transition from triplet state to singlet ground state is called as Phosphorescence.

Applications:

1. Determination of inorganic substances:

Ion	Reagent	Wavelength (nm)		Sensitivity µg/ml
		Excitation	Flourescence	
Al^{3+}	Alizarin garnet	470	500	0.007
Zn^{2+}	Benzoin	-	Green	10.0
Sn^{4+}	Flavonol	400	470	0.1
Li^{+}	8-hydroxy quinoline	370	580	0.2
Be	Naphthoic acid	380	460	2

2. Determination of organic compounds: Aromatic polycyclic hydrocarbons, indoles, naphthols, proteins, plant pigments, steroids

Infrared Spectroscopy:

Principle:

It is the study of absorption of infrared radiation which results in vibrational transitions and it is mainly used for the determination of functional groups. The atoms or group of atoms are connected by bonds .These bonds are analogus to springs. Because of the continuous motion of the molecule, they maintain some vibrations with some frequency. This is called Natural frequency of vibration. In other words, IR spectra is nothing but a finger print of a molecule.

Vibrations:

Types	procedure
1.Stretching vibration	These are the vibrations in which the bond length is altered and they are of two types 1. Symmetrical stretching: two bonds increase or decrease in length 2. Asymmetrical stretching: When one bond length increases and other one decreases

2.Bending vibrations	a. In-plane bending: In these vibrations, there is change in bond angle. Bending of bonds takes place within the same plane i. Scissoring: bond angle decreases ii. Rocking: bond angle is maintained , but both bonds moves with in the plane b.Out of plane bending : i. wagging: Both atoms move to one side of plane ii.Twisting: one atom is above the plane and the other below the plane.

Applications:

1. It is used to determination of functional group and structure elucidation
2. Study of polymer
3. Ratio of Cis –trans isomers in a mixture of compounds
4. The quantity of substance can be determined by either in pure form or as a mixture of 2 or more components.

NMR(Nuclear Magnetic Resonance Spectroscopy):

It is the study of spin changes at the nuclear level when a radio frequency energy is absorbed in the presence of magnetic field.

Principle: By the application of an external magnetic field, the nucleus spin on its own axis and a magnetic moment is created, resulting in precessional orbit, with a frequency called as precessional frequency. In this state the magnetic field caused by the spin of nuclei is aligned with the externally applied magnetic field.

When energy in the form of radiofrequency is applied , absorption of energy occurs ,the nucleus moves from ground state to excited state, which results in Spin reversal or antiparallel orientation.

Applications:

1. It is used to determine the structural elucidation of organic compounds.

2. It is used for the investigation of dynamic properities of the molecules like conformational isomerism, molecular asymmetry , hydrogen bonding, keto-enol tautomerism
3. Determination of optical purity.
4. Study of molecular interaction like micelle formation and drug macro-molecule or drug-receptors interactions.
5. It is used to determine the quantity .
6. Surfactant chain length determination
7. Percentage of hydrogen in the compound can be determined
8. Moisture analysis

Flame Photometry & Atomic Absorption Spectroscopy:

Principle:

Flame emission spectroscopy	Atomic Absorption Spectroscopy
When a solution of metallic salt is sprayed on to a flame(liquid sample) ↓ Formation of droplets ↓ Fine residue and formation of neutral atoms ↓ Excitation of atoms by thermal energy ↓ Emission of radiation of specific wavelength	When a solution of metallic salt is sprayed on to a flame(liquid sample) ↓ Formation of droplets ↓ Fine residue and formation of neutral atoms ↓ Neutral atoms absorb specific wavelength of radiation from hallow cathode lamp ↓ Measurement of intensity of radiation absorbed by using photometric detector

Applications:

Flame photometry	Atomic absorption spectroscopy

It is used to identify the elements in a sample It is used to determine the concentration of calcium in serum, sodium in urine, potassium chloride in syrup Concentration of lithium n serum for therapeutic drug monitorng	Estimation of trace elements in biological fluids Estimation of elements like copper, Nickle, ad zinc in food products Estimation of magnesium, zinc in blood Estimation of mercury in thiomersal solution Estimation of lead in calcium carbonate, petrol Estimation of elements in soil samples, water supply, effluents, ceramics etc